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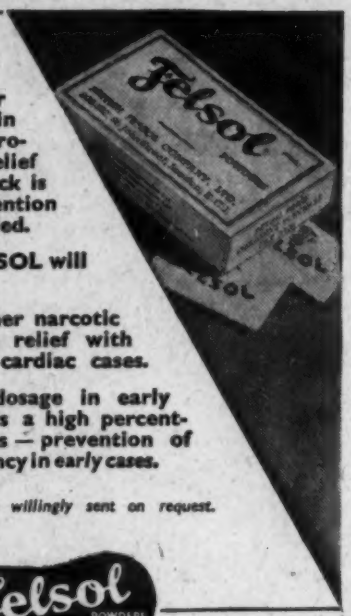

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 26 1943

IMMUNITY TO TUBERCULOSIS*

BY

G. GREGORY KAYNE, M.D., M.R.C.P., D.P.H.

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At the outset we should recognize the immensity of the subject and all its ramifications. We may divide it into natural immunity and acquired immunity, or, more correctly termed, natural resistance and acquired resistance. But, considering natural resistance first, we would need to discuss the influence of race, heredity, sex, and age, and even of different organs and tissues; the difference in resistance, if any, to the human and bovine types of bacillus; and, lastly, the mechanism by which natural resistance is effected. The mechanism of acquired resistance, if indeed it is different, offers an equally important problem, as does the hypersensitivity of the tissues which follows infection. How little do we know about the good influence of various environmental conditions on acquired resistance, and perhaps on natural resistance; and, on the other hand, about the bad influence exerted by malnutrition, intercurrent diseases, childbirth, and certain occupations. And this by no means exhausts the list. What part does resistance play in the development of phthisis as seen in the adult? How far do resistance and hypersensitivity determine the protean characters of tuberculous lesions, the varied clinical manifestations of the disease, and its puzzling epidemiological characteristics? And, finally, there are many problems involved in prophylactic immunization.

There is certainly, as yet, no consensus of opinion on the actual cellular or humoral mechanisms of either natural or acquired resistance among those intimately engaged in such research work. But it is possible to indicate the present trend of opinion on the roles of natural and acquired resistance in the evolution of tuberculosis in man, on the connexion between natural and acquired resistance, and on the relations between the latter and hypersensitivity.

Natural Resistance

Natural resistance has been defined as the inherent ability of the body to restrain the growth and bring about the death of the tubercle bacillus on *first* contact with it. It must have been evident for a long time that such inherent ability is present to a very different degree in different species of animals: rats, for instance, are highly resistant to tuberculosis, as are sheep, goats, and horses. But even in regard to man, "constitution" has since early times been considered to be very important in the development of tuberculosis. The discovery of the tubercle bacillus led to a swing of the pendulum, but the soil soon loomed on the horizon beside the seed. The relative roles of soil and seed in relation to the various manifestations of the disease were not, however, clearly discerned. The discovery of the Koch phenomenon in the guinea-pig gave reality to the concept of acquired resistance; and, translated to man, this concept of acquired resistance following infection has for many years been regarded as all-important in connexion with those tuberculous manifestations that develop some time after the primary infection. Thus, while natural resistance might influence the course of the primary infection, the development of later lesions would be determined by acquired resistance. Acquired resistance would act by killing the bacilli freshly introduced into the body at the site of entrance, generally the lung; or, at least, by limiting the effects of the bacilli to the neighbourhood of this site. Moreover, acquired resistance, as demonstrated in the Koch phenomenon, appeared to act through hypersensitivity of the tissues, which developed at the same time. This hypersensitivity was identified with acquired resistance, and the changed state of the body following primary infection was called "allergy," this term including both resistance and hypersensitivity. Hypersensitivity was also held responsible for liquefaction of the so-called reinfection lesions, with resulting cavitation and bronchial spread. But we meet with difficulties at once. Does natural resistance cease to act and acquired resistance take over? If so, at what stage in the development of primary lesions or afterwards does this occur? Or does natural resistance continue to act? In which case, is acquired resistance merely a reinforcement of natural resistance, or does quite a different mechanism operate with the two? And finally, while we might assume that the principle of the Koch phenomenon is valid for reinfection in man from the outside, does it operate against bacilli derived from incompletely healed lesions in the body? We may recall that in syphilis it does not. What part is played by dosage of virus? There is evidence that no natural or acquired resistance will stand up to really immense numbers of tubercle bacilli. But, all other factors being equal, will natural resistance prove more effective than acquired resistance against large numbers of bacilli? All these questions cannot be answered yet, but observations in man during the past 25 years and further animal investigations have thrown some light on the relations between natural and acquired resistance, and on the role of inheritance in resistance.

Racial Resistance

During the last war it was noted that natives from African communities in which tuberculosis is unknown developed rapidly fatal tuberculosis when they came to Europe. This tuberculosis assumed the so-called childhood or primary type—that is, in addition to the lung lesion, extensive glandular involvement and generalization were found. The facile explanation was accepted that this was due to the fact that these natives had not been infected in childhood and had not therefore developed

* Opening paper in a discussion before the Section of Comparative Medicine of the Royal Society of Medicine, held on Feb. 17, 1943.

acquired resistance. We might, of course, have asked ourselves: If this was indeed the reason, why did not all infected European children die from generalized tuberculosis? However, further observations soon exploded this theory. First there was the work in South Africa among natives on the Rand (Publn. S. Afr. Inst. med. Res., 1932). Although 70% of the natives reacted positively to a very small dose of tuberculin on arrival at the mines they often succumbed to tuberculosis characterized by massive caseation of the tracheo-bronchial glands and extensive caseation of the abdominal glands, liver, and spleen. Yet in 50% of these cases calcified primary lesions were found. Moreover, the disease pursued the same rapidly fatal course whether the reaction to tuberculin was positive or negative on arrival at the mines. On the other hand, it was noted that if the natives stayed in their kraals the disease often remained quiescent. The explanation was offered that the rapidly fatal tuberculosis was due to overwork, undernourishment, and unaccustomed conditions in the mines. But this clearly could not explain it all, since not merely the outcome of the disease but its type was so different from what we see among civilized communities.

Then there are the findings in negroes in the U.S.A. The mortality rate among them is three to four times that among the white population. Moreover, Pinner and Kasper (1932), in comparing the pathological characters of tuberculosis in the negro and the white man, found that the primary type of tuberculosis with caseation of the hilar glands was present in nearly one-half of the negro adults. Yet Opie (1924) had shown that the incidence of calcified lesions among negroes is only slightly less than among white men. Here, too, environmental conditions were blamed for the rapidly fatal course of the disease; but, as already indicated when speaking of South African natives, environment could not account for the different type of tuberculosis; and, indeed, comparisons of negro and white populations, when the living conditions of the whites were certainly no better than those of the negroes, showed the same difference. Thus, although the role of environment cannot be entirely ruled out in these comparisons, there can be little doubt that a racial difference in resistance to tuberculosis exists, and that in negroes this difference shows itself by their inability to develop acquired resistance which would alter the character of reinfection lesions. In other words, if a negro overcomes his first infection he behaves to a later introduction of tubercle bacilli into the body as if it were a first infection. Thus the ability to develop and to maintain acquired resistance can form an integral part of what we call natural resistance.

In this connexion it is of interest to mention some observations of Lurie (1928). It is well known that rabbits are susceptible to the bovine bacillus and resistant to the human bacillus. Yet Lurie found that not only do human tubercle bacilli multiply readily in the rabbit but in the first week after inoculation they grow even more rapidly than the bovine organisms. Whereas, however, the human bacilli are soon destroyed by acquired resistance and the animal recovers, the bovine bacilli continue to multiply in the lung and kidneys until the rabbit succumbs to the disease. Therefore, what appears on the surface as the native resistance of the rabbit to the human type of tubercle bacillus really results from a specific resistance acquired during the progress of the infection; for at first no effective opposition to the multiplication of this organism exists. But it may well be asked, Why is this resistance not acquired against the bovine type of bacillus?

Individual Resistance

We have seen that there is evidence for a racial difference in resistance to tuberculosis. It is widely recognized that there are also differences in resistance among individuals of the same race, even among the highly sensitive guinea-pigs. Thus it is not rare to find among tuberculous negroes the typical phthisis of white people. All investigations relating to individual resistance and inheritance are exceptionally difficult, however, because it is impossible to rule out environmental differences. Even the similarities as regards tuberculosis among the identical twins studied by Diehl and von Verschuer (1933, 1937) might be explained by the fact that such twins are more likely than non-identical twins to have an identical environment. Recent experimental work of Lurie (1941) is highly significant in this connexion. He studied the tuberculosis resulting from various modes of infection in generation after generation of six rabbit families inbred by brother-sister or parent-offspring mating and maintained under uniform environmental conditions. The six families fell into three groups—uniformly highly resistant, uniformly highly susceptible, and others intermediate in resistance. The resistance was found to be a function of genetic constitution which by itself determined whether under given conditions of natural respiratory contagion rabbits acquired (*a*) rapidly progressive primary generalized tuberculosis; (*b*) localized chronic ulcerative pulmonary tuberculosis, corresponding to bronchogenic tuberculosis, the common type seen in the human adult; or (*c*) a disease of a character intermediate between these two extremes. It is significant, however, that the resistance even of the most resistant strains could be overwhelmed by large doses of bacilli.

Apart from indicating the hereditary character of susceptibility to tuberculosis, these investigations appear to show that so-called natural resistance as well as acquired resistance may influence the type of lesion formed on first contact with tuberculosis; and thus they lead to the deduction that acquired resistance is but a reinforcement of natural resistance. Some authors in America (Israel *et al.*, 1941), no doubt influenced by these results, have postulated that apparent differences in the clinical manifestations of primary tuberculosis noted between adults in America and those in Scandinavian countries were due to a genetically higher resistance in North Americans. But, in the first place, it has not been established that the so-called different clinical manifestations of primary tuberculosis are really associated with a different pathological picture of primary tuberculosis: the pleural effusions or the apical infiltrations considered "primary" manifestations by the American workers did not occur soon enough after a change in tuberculin reaction to exclude the possibility that they developed after an insignificant but true primary complex. And, secondly, it seems very doubtful if we are justified in applying results obtained in rabbits by mating of an intimacy unknown among civilized human beings to the interpretation of factors influencing tuberculosis in man. Nevertheless, summarizing all that I have said, we may perhaps, on a broad biological basis, consider that resistance to tuberculosis might show itself in the following degrees. The lowest degree of natural resistance will not, on first contact with the bacillus, prevent an extensive primary complex with rapid generalization and death. A higher degree of natural resistance will lead to a primary complex with perhaps some dissemination, and recovery, but no acquired resistance, will follow; so that, as is the case with negroes and South African natives, described above, a fresh infection under bad environmental conditions will again result in a primary complex, this time with generalization and death. A still higher degree of natural resistance will cause a primary complex, recovery from which will give acquired resistance; and therefore any subsequent reinfection will not produce a primary complex but a parenchymatous lesion which tends to liquefy, cavitate, and spread by the bronchi. People still more naturally resistant might conceivably react to a first infection by developing the latter type of lesion at once, as postulated by some American workers. This concept, which, I emphasize, must for the present be considered as largely theoretical, involves one important assumption: that acquired resistance is the same as natural resistance, which it enforces, and that presumably when either natural resistance or a combination of natural plus acquired resistance reaches a certain level, hypersensitivity appears, causing liquefaction and cavitation. One supporting fact to be mentioned is that it is not extremely rare to meet with liquefaction of a primary pulmonary focus.

Allergy

This brings me to the phenomenon of hypersensitivity. The term "allergy," as originally coined, was applied to the difference between the body's response to a second or later dose of antigen (the tubercle bacillus or its products) and its response to the *first* introduction of the antigen. The term has been identified with hypersensitivity as shown in the Koch phenomenon and the tuberculin test. Resistance gained from a primary infection was considered to be due to this hypersensitivity, or at least to run parallel with it and be inseparable from it. These views have been greatly altered as a result

of the work of Rice Rich (1936) and his associates. As he puts it: "For many years it has been generally believed that the state of hypersensitivity is the chief mechanism of acquired immunity, the accentuated allergic inflammation having been regarded as the means by which the growth and spread of the bacilli are inhibited. The dangerous and destructive effects of hypersensitive reactions have always been very clearly recognized, but they were believed to be necessary evils that had unfortunately to be borne if one were to possess any acquired resistance at all." Rich, in experiments which are well known, succeeded in separating resistance from hypersensitivity. It has been shown that acquired resistance could be established without concomitant development of hypersensitivity; thus Pagel (1937) states that by treating animals with heat-killed tubercle bacilli he has produced immunity without hypersensitivity; and that (Pagel, 1936) such animals developed bronchogenic tuberculosis (the type comparable to phthisis in the adult) after virulent infection. It has also been shown that acquired resistance of a resistant hypersensitive animal could be transferred passively to a normal animal without concomitant transfer of hypersensitivity; and, finally, that when the hypersensitivity of a resistant animal was abolished by desensitization resistance remained intact. Nevertheless, it is probable that allergic inflammation enforces resistance by bringing to the site of reinfection, more quickly and in more concentrated form, factors that tend to fix the bacilli *in situ* and promote their destruction. It is generally agreed that allergy largely results from stimulation of the tissues by an antigenic component of the tubercle bacillus. Whereas, however, some believe that this component is different from that responsible for the production of resistance, others, like Pagel (1939), consider that hypersensitivity develops when antigen is in excess of antibody, and that this leads to tissue destruction with liberation of antibodies; while resistance due to surplus of antibodies causes no destruction of tissues. At all events, even if allergy is not an essential factor in the mechanism of resistance it appears to have a deep influence on the development of the disease in man.

Mention of the dissociation of resistance and hypersensitivity brings me to the tuberculin test. Allergy or hypersensitivity to the tubercle bacillus should not be identified with tuberculin hypersensitivity. The latter phenomenon appears to be quite unconnected with resistance, and its exact mechanism is still obscure, although our knowledge has advanced as a result of the work of Seibert and her associates. The tuberculin reaction does not represent anaphylactic sensitization to foreign protein, for in the latter phenomenon there is interaction of demonstrable antibodies with antigen, and sensitization of the cell cannot be demonstrated. The tuberculin reaction, on the other hand, is the result of sensitization of the cell itself, and antibodies cannot be demonstrated. The active principle responsible for the skin reaction is apparently protein in nature, and the origin of tuberculin hypersensitivity is connected with the tuberculous lesion; thus hypersensitivity tends to increase with extension of the lesion and to disappear with complete healing. It has even been shown that it is more marked in proximity to the lesion than in the body generally.

In view of what has just been said it is perhaps not surprising that tuberculin tests, both in clinical and in epidemiological work, sometimes give unexpected results. Those who condemn the test on these grounds should at least make sure that they use the purest material available—at present P.P.D.—prepared under rigid standards, and employ similar standards in carrying out and reading the test. Even when all this is done we may still find unexplained variations in the degree of hypersensitivity, or its absence, in persons who have certainly been infected. This should, however, spur us on to further work in order to elucidate this important phenomenon. For it seems clear that it is on the understanding of resistance and related phenomena that the future of tuberculosis control rests.

Mechanism of Resistance

I cannot conclude without referring to the intimate mechanism of resistance to tuberculosis, although I realize that I shall be entering, inadequately equipped, territory much explored yet little charted. Briefly what we have to ask is, What is the fate of the tubercle bacilli, and what part is played in this fate by cellular and by humoral factors?; and we must ask these questions in regard both to natural and to acquired resistance. According to Pagel (1940, 1942) the fate of bacilli in natural resistance is represented by what happens to them when injected intradermally into the mouse. First the bacilli lose their envelope, being converted from basophilic into eosinophilic organisms; then they become granular and gradually disappear. Or they may remain indefinitely at the site of inoculation without multiplying. The fate of bacilli with acquired resistance, as represented in the Koch phenomenon, is quite different. They disappear rapidly—within a few days or even hours; a few small granules are all that remain. Tubercles form quickly—in from two to four days. The bacillus is now treated as a foreign body that cannot be absorbed, and the tubercles act as a barrier shutting off the bacilli from the rest of the body and the circulation.

Next we come to the thorny and still unsettled question of the relative importance of cellular and humoral factors. Pagel considers that the role of the cells is unimportant, if indeed they play any part at all, in connexion with both natural and acquired resistance. On the other hand, according to Lurie, a very important part is played by the mononuclear phagocytes. Pagel maintains, however, that earlier experiments by Lurie himself contradict this conclusion. At the same time, it must be emphasized that no bactericidal power has been demonstrated in the serum of animals either naturally resistant or made so as a result of infection.

There is one final point I cannot resist making. When I was consulting the Society's *Proceedings* I came across a discussion in 1925 on the control of tuberculosis and the milk supply. I read there the same emphatic evidence that is brought forward to-day by those who appreciate the seriousness of the problem, and, on the other hand, the same arguments against the pasteurization and boiling of milk, and the same expression of difficulties associated with eradicating the disease in cattle. It was more than disheartening to conclude that apparently little, if anything, had been done about it all since then. But I also heard one tuberculosis authority maintain, among others, that he was definitely convinced of the importance of partial immunization against pulmonary tuberculosis as a result of the ingestion of small numbers of bovine tubercle bacilli in milk, and, moreover, that he regarded this as one of the causes underlying the favourable alteration in clinical type and in death rate from human tuberculosis noted in recent years. I do hope that, in view of the present discussions on the safety of the milk supply, this view is no longer held by any responsible member of our professions, and that such travesty of one aspect of immunity will not be allowed to hinder an effective campaign for the eradication of tuberculosis in cattle.

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Dr. Charles B. Huggins, professor of surgery at the University of Chicago, has been awarded a prize of $2,000 given by Dr. Charles L. Mayer and administered by the National Science Fund of the National Academy of Sciences. The prize was offered for the most outstanding contribution made during 1942 to present-day knowledge of factors affecting the growth of animal cells, with particular reference to human cancer. The advisory committee decided that this award should go to Dr. Huggins for his studies of the human prostate, with special relation to the cancers taking origin from this gland. A second Charles L. Mayer prize of $2,000 for an outstanding study made in the same field in 1943 will be given, and entries and recommendations for this award should reach the office of the National Science Fund, 515, Madison Avenue, New York City, by Jan. 15, 1944. The advisory committee is interested primarily in fundamental studies on the factors influencing growth of animal cells rather than applications to any particular aspect of normal or abnormal growth.

MILD DEPRESSIVE PSYCHOSIS

BY

B. ANDRATSCHKE, M.D.Prague

AND

C. H. ROGERSON, M.D., M.R.C.P., D.P.M.

(*From the Cassel Hospital for Functional Nervous Disorders*)

In a recent paper upon the health of the doctor, Hope Gosse (1942) gave a table showing the relative frequency of various conditions which had been the cause of sickness of more than seven days' duration in a large group of doctors. The diagnosis "anxiety state" appeared fifth on this list, being more frequent, for example, than appendicitis, peptic ulcer, or cardiovascular disease. Gosse did not claim that this was especially a doctor's disease, so that similar findings might be expected from many other groups of people. The context of his table suggests that the term "anxiety state" was used to cover a wide range of psychiatric conditions not amounting to insanity. His findings agree with the clinical observations of others that functional nervous disorders of this type account for a very large annual wastage through sickness. Indeed, the incidence may be even higher than that stated, since it is notorious that physical diagnostic labels tend to be used in preference to psychological ones wherever possible.

Among the cases thus loosely designated would undoubtedly be found a number of different types. The Cassel Hospital, which was founded to provide treatment for such functional nervous disorders, can furnish from its records evidence of what these types are and which of them are preponderant. A study of these records shows that the majority of cases are grouped under three diagnostic headings. In 1938, for example, out of 137 total admissions there were 45 cases of depression, 35 of anxiety neurosis, and 22 of hysteria. Under all other diagnostic headings together there were 35 cases. Depression was thus the commonest, and it was also the most painful and, owing to suicidal risk, the most dangerous condition requiring hospital treatment.

Lewis (1938) has defined a depression as follows: "Any person who is unhappy and ill with his unhappiness may properly be said to be in a state of depression." In this phrase he has caught the essence of the condition—the symptoms presented by the patient are dependent upon the disorder of mood, which is fundamental. It may be misleading in one sense, however, in that the patient does not invariably complain of his unhappiness but often only of the symptoms consequent upon it. A depression may be said to be psychotic in character, and hence to belong to the group under discussion, when it occurs in the absence of any discoverable psychological trauma, becomes disproportionate to the trauma, or persists unduly when the trauma has ceased to operate.

The treatment of the common functional nervous disorders, including mild psychotic depression, was admirably laid down by T. A. Ross (1937). He dealt most fully with the anxiety neurosis and the hysterical reaction, and his methods still form the basis of the most successful and widely used therapy. Towards depression, however, he was more cautious in his attitude, holding that treatment could increase the comfort of the patient but could not radically affect the course of the illness. Lewis (1934), at the conclusion of his masterly historical review of the subject, expressed similar views:

> "There has been very little written in this review as to therapeutics. Notable as have been the changes in the general care of the insane, there is little to be said about the particular treatment of depressive states. To hinder suicide, to prevent irritation, and to provide for nutrition, sleep, or rest and in due course occupation and interests have long been the objects of judicious treatment, conscious that of the factors potent to heal time is more important than any kind of interference so far attempted."

The position to-day is widely different. The introduction of shock therapy for the treatment of depression has produced a revolution in psychiatric therapy which is still not sufficiently appreciated. In most cases this treatment is capable of cutting short the attack within the space of three or four weeks. It is of outstanding value in the mild non-certifiable types of depression which are so often encountered in clinical practice and in the case material of the Cassel Hospital. Remission rates for all types of depression quoted by various authors—e.g., Hemphill (1942) and Sands and Sargant (1942)—are very high. It must of course be remembered that these cases usually recover spontaneously in the end, but the time and misery saved by effective treatment are very great.

This being so, the early recognition of the mild depressive reaction becomes of the utmost importance, more especially since it appears to be true that the earlier the treatment is begun the more rapidly the remission occurs. Clinical experience in this hospital has led us to the conclusion that in very many cases recognition comes, if at all, much too late. We have therefore felt it advisable to set forth a description of the mild depressive reaction as it has come to our observation, in the hope that it may assist others to detect it.

Survey of 100 Consecutive Cases

It may at first sight appear to be a curious procedure to present a picture of an illness including only so-called mild examples. Our justification is that we have found that these are precisely the cases which present the greatest difficulty and occur with the greatest frequency in general practice. The personality is well preserved, delusions are absent, and the practitioner who has learned to recognize severe examples of the manic-depressive psychosis may fail altogether to recognize these cases for what they really are. It is as if the physician who has observed a severe streptococcal bronchopneumonia should fail to appreciate that a streptococcal sore throat is also a respiratory infection which may require similar treatment. All of our cases were mild ones in the sense that they were not certifiable or acutely suicidal, and they were able to live in the relatively open environment of the Cassel Hospital. In the sense of degree of incapacity produced by the illness they were not in most cases mild at all.

Our survey covers 100 consecutive cases of mild psychotic depression admitted to this hospital between 1939 and 1942. Our aim has been to present so far as is possible a review of the typical history, symptomatology, and characteristic features of the illness in order to facilitate its recognition by the busy practitioner who has little time for psychiatric niceties.

Diagnosis on Admission

It may be of interest to record the diagnoses with which these patients were sent to hospital. The majority were referred by general practitioners or non-psychiatric consultants, a minority by psychiatrists. A diagnosis of depression was made in 25% of cases; 32% were classed as anxiety neurosis, 14% as neurasthenia or psychasthenia; in 15% no diagnosis was proffered. In the other 13% a heterogeneous series of diagnoses were made, including hysteria 4%, schizophrenia 3%, phobia, obsessional neurosis, etc.

Had we any right to assume that in these cases our diagnosis was the correct one? There can be no hard-and-fast criteria in psychiatry, no infallible signs to guide one to the proper diagnosis. On the other hand we had several advantages over our colleagues who referred the cases to us: we were able to study them for a considerable period in detail, we had them under observation for 24 hours of the day, and we received daily reports from a trained nursing staff. Moreover, when there was doubt about the diagnosis the ultimate grouping depended upon the combined opinion of at least three psychiatrists. We believe that, given the same opportunity for observation, our fellow psychiatrists would have reached the same conclusion as ourselves in nearly every case. The problem of differential diagnosis will be discussed later.

Sex, Age, Occupation

Of our patients 56 were males, 44 were females. There is no evidence from these figures of any sex predisposition, a fact which is confirmed by others (e.g., Rennie, 1942). Age distribution is shown in Table I. There is no special occupational bias: employment covers the whole range of occupation usually met with at the hospital. It is, however, noteworthy that with few exceptions all these patients were usefully employed before

their illness and were often living particularly full and productive lives. This fact would be less often observed in a similar group of anxiety neuroses or hysterical reactions. Ross has emphasized this point.

TABLE I.—*100 Cases of Depression. Age on Admission and at First Attack*

Age	On Admission			First Attack		
	Males	Females	Total	Males	Females	Total
Under 20 ..	2	1	3	13	5	18
20–29 ..	4	9	13	11	15	26
30–39 ..	12	11	23	14	9	23
40–49 ..	11	12	23	6	11	17
50–59 ..	19	7	26	8	3	11
60 ..	8	4	12	4	1	5
Totals ..	56	44	100	56	44	100

Symptomatology

In Table II are shown the leading complaints of our patients at the time of admission. It will be noted that only 58% actually complained of feeling depressed. Almost all of them subsequently admitted such feelings in response to definite leading questions, but we are here concerned with the spontaneous observations of the patients themselves. Physical symptoms figured among the leading complaints in 78% of cases. There was a variety of such complaints, ranging from insomnia, fatigue, headache, loss of appetite, constipation, palpitation, to all kinds of strange feelings—i.e., tension in the spine, peculiar feelings in the skin, tightness in the head, etc. Only 10 of these patients presented a single physical symptom; in all other cases complaints were made of a number of physical symptoms.

TABLE II.—*100 Cases of Depression. Frequency of Occurrence of Leading Symptoms*

	Males	Females	Total
Physical symptoms	40	38	78
Depression	38	20	58
Fear, anxiety, agitation	30	17	47
Feeling of inadequacy	26	19	45
Feeling of guilt or unworthiness ..	9	10	19
Perplexity or unreality	—	10	10
Suicidal thoughts	4	4	8

Next in frequency came a group of complaints of "fear," "anxiety," "agitation," etc. The most common fear was of becoming insane; other fears were of death, of cancer, of meeting people, etc. Nearly half of the patients complained of a feeling of inadequacy, expressed in various ways—e.g., incompetence, the mind not working as it formerly did, inability to carry on with duties properly, etc. Feelings of guilt and unworthiness—of not being good enough for one's family, of having committed terrible mistakes, etc.—occurred in 19%. Feelings of unreality or perplexity were found in 10%: it is interesting to observe that these patients were all women. Suicidal thoughts were mentioned in only 8% of cases, but, as with the complaint of depression, many more had experienced such ideas than mentioned them at the first interview.

Absence of hallucinations, delusions, etc., is to be explained by the nature of the group of cases we are here studying.

Previous Personality

A study of the previous personality of our patients reveals some interesting observations. Though the descriptions were recorded by a number of different observers working largely independently, three groups of cases emerge quite clearly. The first and largest contains 44 patients, all of whom were described in terms stating or implying overconscientiousness and a tendency to perfectionism in all their actions. Of these, 12 were also possessed of great drive, and were as a rule definite leaders in their own sphere; 7 were also described as timid and fearful, and these were on the whole overwhelmed by their own conscientiousness. The second group contains 13 patients whose normal personality was gloomy and pessimistic; in addition they were more or less hypochondriacal. In contrast to these two groups was a third, totalling 11 cases, in which the personality was described as cheerful, "outgoing," and either placid or active. It is worth noting at this point that out of a total of 9 manic attacks in the life histories of the whole series 7 (each single attacks) occurred in this small group. These were in fact evidently the true manic-depressives, whose physique and temperament have been described by Kretschmer (1936). Unfortunately we have not sufficiently reliable data on the physique of these patients.

The rest of our series was a heterogeneous one including 8 whose previous personality was frankly inadequate, 5 unstable psychopaths, 2 paranoiacs, and 17 in whom no special features were noted.

Precipitating Factors

Precipitating factors, mainly of psychological but to a small extent of physical or mixed origin, were found in 82% of cases. These figures correspond closely with Rennie's observations. Psychological factors were represented by conditions or events which would place a special strain upon the individual. In Table III distinction has been drawn between acute psychological stress or trauma—in our cases mainly the death of a parent or marriage partner—and chronic psychological stress, which seems to play a more important part, being present in 62 cases. The commonest sources of such stress were business and professional worries and marital difficulties.

TABLE III.—*100 Cases of Depression. Precipitating Factors*

Chronic stress* alone	38
Plus acute stress	10
Plus physical disease	14
Acute stress alone	11
Plus physical disease	4
Physical disease alone	5
Total with precipitating factors	82
„ without known precipitating factors	18
Total	100

* "Stress" = psychological stress.

Physical disease, either alone or in connexion with acute or chronic psychological stress, appeared in 23 cases. Of these 7 had focal sepsis in teeth, tonsils, or sinuses, 9 had had influenza, and two presented degenerative cardiovascular disease. There were no examples of frank endocrine disorder, though involutional factors were thought to be present in 5 cases.

The war as a source of chronic stress (i.e., aggravation of business or personal worries, anxiety and loss of sleep due to air raids) played an indirect part in 26 cases. In 2 cases it appeared to be directly responsible through the patients' personal experience of an air-raid disaster.

History of Previous Attacks of Depression

Out of the 100 cases 51 had had one or more previous attacks of depression before their admission to hospital. The figures are necessarily approximate, since one often had to rely upon the descriptions given by patients or their relatives. The age at onset of all first attacks is shown in the second part of Table I. The peak occurs in the 20–29 age group. A surprisingly large number of first attacks happened at or before the age of 20. With one doubtful exception all these occurred after puberty. Of the 61 patients over the age of 40 admitted to hospital 33 had had previous attacks. This figure corresponds closely with clinical experience, and it may be said with confidence that of all patients over 40 seen in an attack of depression at least half may be expected to have had one or more previous attacks.

Family History

Findings concerning family history are shown in Table IV. They are based upon 83 cases, since in 17 no record of the family history was found. Records concerned first- and second-degree relatives, with the addition of data about first cousins

TABLE IV.—*100 Cases of Depression. Analysis of Family Histories*

Recorded histories	83
With abnormality	62
Without „	21

Disorder	Total Cases Recorded in 87 Histories	Rate per 100 Family Histories
Depression	13	15·7
Suicide	14	16·9
In mental hospital	18	21·7
Neurotic, unstable, etc.	44	53·0

in two cases. For convenience the number of abnormal individuals per 100 family histories is presented in column 2 of the table. It will be observed that the number of relatives who have had a serious attack of depression, had been in a mental hospital, or had committed suicide is such as to give a combined rate of 54.3 per 100 family histories. This figure may convey some idea of the degree of taint in the family histories of cases of depression and of the frequency with which positive findings may be anticipated.

Differential Diagnosis

We are now in a position to build up the picture of a typical case of mild depression as it may be met with in clinical practice. Among the commonest positive features are the following:

The patient may be of either sex and any age past puberty. In three-quarters of the cases one of the leading complaints will be of physical symptoms, nearly always multitudinous and often rather unusual. In approximately half the cases there will be a complaint of depression, anxiety, or feelings of inadequacy, often of all these things. In half the cases the patient will have been of a conscientious perfectionist nature—very often before his illness a successful individual, though occasionally overwhelmed by his own conscientiousness. Three-quarters of the cases will show definite precipitating factors of a psychological kind. Chronic stress will be found much more frequently than acute disaster. About a quarter of the cases will present physical precipitating factors; among these, sepsis and influenza are worthy of note. Half the patients over 40 years of age will have had a similar attack in the past. The family histories will frequently include one or more relatives who have had an attack of depression, have been in a mental hospital, or have committed suicide.

In addition to these positive findings there are certain others which are very characteristic of the depressive attack but less easy to present in statistical form. There is often a tendency towards a diurnal rhythm: the patient is worse in the morning and better in the afternoon or evening. Insomnia is common; the patient can usually get off to sleep promptly, but awakes very early. Loss of weight, amenorrhoea, and lack of sexual feeling are also frequent. The weight curve is usually a reliable guide to the progress of the attack. Lastly, the depressed patient tends to have a special attitude towards himself and his symptoms. He feels so unworthy that he almost apologizes for taking up the doctor's time. This is in marked contrast to the neurotic patient, who generally revels in his own symptoms and expects the physician to be as interested in them as he is himself.

The above positive findings, taken singly, will not furnish much evidence of the nature of the attack, but where several are found in one case (and their frequency is such that more than one is likely to be found in each case of depression) they provide strong pointers to the correct diagnosis. Since, however, no mere mathematical sum of clinical facts is sufficient in itself to enable one to arrive at a diagnosis it is necessary to add certain observations of a more general character.

Anxiety neurosis was the diagnosis most frequently made before admission. Indeed, complaints of anxiety, agitation, and fear were often so prominent as to mask the underlying state of depression. The genuine anxiety neurosis tends to be of two types—an acute form in which each individual attack of anxiety develops abruptly, lasts for a few minutes or a few hours, and then dies away; and a more chronic form, often termed neurasthenia, in which smouldering symptoms of anxiety are almost constantly present. In both types psychodynamic factors can always be found which have an immediate cause-and-effect relationship to the anxiety symptoms. In the acute type the situation in which the attack occurs, or some association which that situation arouses, is usually pregnant with meaning for the patient and provides the clue to his repressed fears. In the chronic type there may be a more diffuse and complex cause for the symptoms, based upon faulty mental habits, with unhealthy attitudes towards himself, excessive timidity, etc. In both types depression occurs as well as anxiety, but it also is dependent upon situational factors—in contrast to the mood of a true depressive psychosis, which is far less affected by environmental changes.

In the history of a typical anxiety neurosis the symptoms will be found to have a gradual progressive evolution in the life history of the patient. The neuroses have been termed by Gillespie (1942) "disorders of social relationships," and this phrase illuminates most aptly their essential distinction from psychotic depression, which is an illness occurring as a more definite and circumscribed entity in the life history of an individual who at other times may appear relatively well adjusted.

The differential diagnosis from schizophrenia is usually evident from the bizarre nature of the symptoms in this condition and the previously shut-in nature of the schizophrenic personality. Difficulty chiefly arises at the two opposite poles of adult life—in adolescence and at the involutional period, when depression often assumes an unusual character. Discussion of these problems, however, belongs to the psychiatric textbooks.

It is necessary to bear in mind that depression produces a lowering of the whole psychic efficiency of the individual, so that, for example, obsessional symptoms may make their appearance. When such symptoms occur in attack form it is always wise to consider the possibility of an underlying depression.

Course and Treatment

It is difficult to predict the probable duration of an untreated attack of depression. A few cases clear up very quickly, lasting only a few days or a few weeks. The majority last for several months, a few very much longer. In the present series the longest duration was 7 years, and there were one or two others with a duration of 3 or 4 years.

Without shock therapy remission is generally a gradual process. The weight begins to improve, appetite to return, insomnia to lessen. There are often brief spells of cheerfulness to break the gloom, which seems by contrast all the worse. Indeed, it is sometimes then that suicidal risk is greatest, particularly as the power of decision is returning to the mind. Occasionally there is a sudden abrupt remission in some quite incongruous situation. Occasionally also there may be a swing over to a state of elation and excitement. Minor hypomanic episodes are fairly common, but they are usually transient and easy to handle. More severe examples are rare in this group, as may be inferred from the fact that there was a history of only 9 manic attacks during the previous life of all these patients. The misery which these patients experience during their illness has in the past only served to emphasize the inability of the physician to provide any specific remedy. General measures as emphasized by Ross and by Lewis have played their part as in many other conditions, but recovery, when it has occurred, has often been ascribed by the patient to some quite fortuitous circumstances.

There can be little doubt in the minds of those who have observed any considerable series of results that convulsion therapy provides the means, so long sought, of cutting short the attack of depression. The theoretical basis for the treatment is almost non-existent. It was introduced by von Meduna for the treatment of schizophrenia. Experience suggests that it is in fact not the treatment of choice for schizophrenia, but that it should be reserved mainly for depression. Cardiazol was at first used to induce a convulsion; but it is unpleasant for the patient, and the risk of fractures during treatment is considerable. Electric-shock therapy, credit for the introduction of which to this country must be shared between Fleming, Golla, and Grey Walter (1939) and Shepley and McGregor (1939), is rapidly superseding it. This method is without unpleasantness save for the transient disturbance of memory, and the risks are very slight. At this hospital, for example, about 400 convulsions have been induced during the past 12 months without serious misadventure. The majority of mild depressions, even those of several years' duration, are relieved by 3 to 8 convulsions, administered twice weekly. In many cases the improvement after two treatments is dramatic in the extreme.

In suitable cases treatment can be undertaken in the out-patient department or consulting-room. However, there is one point that must not be overlooked: treatment is not finished when the attack of depression has been overcome. The majority of cases have had some important psychological precipitating factor. It is necessary to attempt to deal with this factor, lest relapse occur speedily. This may require quite extensive psychotherapy or, more commonly, an attempt to

instil into the patient's mind certain principles of mental hygiene which he had previously ignored. The importance of the constitutional factor must not be forgotten; but this should only emphasize the need for the patient to live within the limits of his capacity. There is no evidence that convulsion therapy has any power to prevent the recurrence of depression in the future. Experience over many years has, however, taught us that mental hygiene, sensibly applied, can greatly influence the probability of relapse.

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ABNORMAL AGGLUTINATION REACTIONS OF A STRAIN OF LEPTOSPIRA ICTEROHAEMORRHAGIAE

BY

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Proof of the diagnosis of Weil's disease (spirochaetal jaundice) depends in most instances on serological investigation. It is often impossible to differentiate this condition, on clinical grounds alone, from infective hepatitis (catarrhal jaundice), and only on rare occasions are leptospira seen in the blood or isolated by culture or guinea-pig inoculation during the first few days of the disease. Most commonly, Weil's disease is suspected because the patient, by vocation or chance, is brought into contact with rats (e.g., working in sewers, damp mines, fish-markets; immersion in canals or stagnant pools). Confirmation is obtained from the blood count, which in Weil's disease shows a polymorphonuclear leucocytosis; and proof is furnished by the presence in the serum of increasing amounts of antibody to *Leptospira icterohaemorrhagiae*.

The agglutination test is generally used to detect the presence of antibodies, and the specificity of the reaction has been well established, although care is needed in the choice of strain, preparation of antigenic suspension, and interpretation of results (Brown and Broom, 1939). In our case, for routine tests we chose, after a considerable amount of experimental work, a strain of *L. icterohaemorrhagiae* (Jackson) which we isolated in 1934 from a London sewer-worker suffering from Weil's disease. Cultures of this strain, grown in Fletcher's rabbit-serum-broth medium and formalinized to 0.2%, were used for eight years. This strain proved satisfactory throughout that period as judged by the correlation between the agglutination results and the clinical histories, blood pictures, and (in positive cases) the occasional isolation of leptospira from the blood or urine of patients.

Recent Abnormal Reactions

During the autumn of 1942, however, the sera of 34 cases of jaundice admitted to the Cambridge Hospital, Aldershot, were found to agglutinate this strain of *L. icterohaemorrhagiae* although there was nothing in the history of these patients to suggest that they were suffering from Weil's disease. In addition, differential blood counts were either normal or showed a relative mononuclear increase, as occurs in infective hepatitis, instead of the polymorphonuclear leucocytosis characteristic of leptospirosis. Nevertheless, these sera produced a true agglutination of *L. icterohaemorrhagiae* (Jackson). The agglutinated clumps, examined by dark-field illumination with a 1/12-in. objective, proved to consist of leptospira, thus differing from the false agglutination referred to by Brown and Broom (1939). During the course of the disease in these patients the agglutination titre of the serum rose to a limited extent (titres of 1/300 were not unusual) and then disappeared completely in a few weeks. In true Weil's disease the titre commonly reaches 1/10,000 to 1/30,000, and remains demonstrable, though at a lower level, for years after recovery.

The occurrence of a positive agglutination and the rise in titre during the disease suggested the possibility of atypical Weil's disease. Centrifuged deposits from the urine of patients between the fifteenth and twenty-third days of disease were examined microscopically by dark-field illumination, and were scarified into guinea-pigs by Lieut.-Col. N. T. Whitehead, R.A.M.C. All precautions were of course taken to examine as fresh urine as possible; and alkalis were administered to the patients to render the urine slightly alkaline. Blood taken from patients during the first ten days of the disease was also inoculated into guinea-pigs. In no case were leptospira seen and no guinea-pig became infected.

Protection Tests

The serum from cases of Weil's disease will normally protect guinea-pigs against infection by a virulent strain of leptospira. Pooled serum from six of the Aldershot cases was therefore injected intraperitioneally into guinea-pigs, each animal receiving a single dose of 5 c.cm., 2.5 c.cm., or 1 c.cm. The same doses of known anti-leptospira serum were given to another series of guinea-pigs. All the animals, and also controls which had received no serum, were inoculated with 0.5 c.cm. of a virulent culture of *L. icterohaemorrhagiae* (W.P.R.L. strain). The temperature of each animal was taken and recorded daily.

The results of this experiment were unusually clear-cut for a protection test. The anti-leptospira serum protected all the animals, none of which showed even a rise of temperature. The control guinea-pigs and all those which had received the pooled Aldershot serum showed the accustomed signs of leptospirosis in guinea-pigs—namely, temperatures mounting to 106° F. followed by a sudden fall to subnormal, and terminated by death between the fifth and seventh days. Post mortem the appearances were typical, and leptospira were seen in microscopical preparations from the livers.

Further Tests

Additional serological tests were carried out with other strains of *L. icterohaemorrhagiae*—namely, one human strain (Coppard) and two rat strains (Wild Rat and W.P.R.L.), all of which agglutinate well with anti-leptospira sera. The sera under investigation failed to agglutinate these strains. In addition, the adhesion test described by Brown and Davis (1927) was applied to these sera. The same strain (Jackson) which gave the spurious original agglutination results was used, but as a living, not a formalinized, culture. The adhesion test was consistently negative with these sera. These serological tests were carried out in duplicate, independently, in London and Aldershot, and only insignificant quantitative differences were obtained by the two workers.

It is apparent, therefore, that formalinized suspensions of this particular strain have become unduly sensitive to sera of certain cases of jaundice other than Weil's disease. The effect is not caused by the presence of bile in the serum reducing interfacial tension, because serum from a number of cases, including twelve of arsphenamine jaundice, produced no agglutination.

It seemed possible, therefore, that the result might be due to an altered protein ratio of the serum. We had intended to carry out protein-fractionation of all sera, but unfortunately pressure of other work rendered this impossible. However, to test this point with serum the protein ratio of which was known to be altered, blood from 25 patients suffering from various diseases which produce a high red-cell sedimentation rate was kindly supplied to us by Dr. J. M. Alston. Only one serum agglutinated *L. icterohaemorrhagiae* (Jackson); the others were all negative. The positive serum was from a child with a rheumatic condition; but after a few days in hospital he was removed by his parents and lost sight of.

There was no suggestion, therefore, that the protein changes which produce high E.S.R. are responsible for the agglutination.

Abnormal Behaviour of L. canicola

At this stage in the investigation a paper by Das Gupta (1942) appeared in which he stated that a particular strain of *L. canicola* had recently become agglutinable by normal human serum. Das Gupta found that this non-specific agglutination did not take place if the serum were heated to 56° C. for half an hour before use.

This abnormality differs from the one we have described because the suspensions of *L. canicola* were agglutinated by normal serum. However, we retested several samples of the sera under investigation against the Jackson strain after they had been heated. The agglutination titres were reduced but not abolished. This reduction of titre is not due to destruction of complement, because sera which had been held at room temperature for periods up to six weeks still produced agglutination, and after that time no complement could have been present.

Reversion of L. icterohaemorrhagiae to Normal

The leptospira suspensions with which these investigations were carried out were prepared from serial subcultures of the strain, and the aberrant agglutinations occurred with the different lots in use from Sept. to Nov., 1942. Later in November it was realized that no further sera which were without effect on the other strains were agglutinating the Jackson strain. Samples of four sera which previously agglutinated the strain were still available and were retested. Now they also produced no agglutination. Since that time some 50 additional sera have been tested, but no further cases of non-specific agglutination have occurred. The suspensions, however, are still agglutinable to full titre when tested against immune rabbit serum.

Discussion

The agglutination of one strain of *L. icterohaemorrhagiae* by a number of sera which were negative with other strains, and the abrupt cessation of the phenomenon, seem to point to some temporary instability of this strain. It is of course well known that the agglutinability of strains varies greatly, and this strain was chosen because it agglutinated well. The medium used for culturing leptospira contains rabbit serum, and it sometimes happens that the serum of certain rabbits appears to retard rather than enhance the growth. Also, some apparently satisfactory cultures fail to agglutinate with specific antiserum. It might be argued, therefore, that some abnormality of the medium had produced unduly sensitive suspensions, whereas later subcultures in normal medium had reverted to their usual stability.

On the other hand there is the undoubted fact that the serum from only a proportion of cases of infective hepatitis gave positive results with these suspensions, and this seems to suggest that the sera possessed some unusual constituent which reacted with an abnormally unstable suspension.

Summary and Conclusions

More than 70 cases of jaundice occurring during the autumn of 1942 have been investigated. Of these, the sera of 34 agglutinated the strain of *L. icterohaemorrhagiae* (Jackson) that had been in use for eight years as a diagnostic antigen.

These " positive " sera failed to produce adhesion with the same strain, failed to agglutinate other strains of *L. icterohaemorrhagiae*, and failed to protect guinea-pigs against infection with a virulent culture of leptospira.

No leptospira were seen in the deposits of the centrifuged urine of these cases. Scarification of the deposits and inoculation of blood into guinea-pigs failed to produce infection.

Differential blood counts done on these patients were either normal or showed a relative mononuclear increase instead of the polymorphonuclear leucocytosis characteristic of Weil's disease.

The non-specific agglutinations are different from the false positives we have previously described. In our opinion they are due to an acquired abnormal susceptibility of the strain used as the antigen.

This instability was lost on further subculture, and the strain has apparently reverted to normal.

There must have been some additional factor present in the serum, because the sera of only a proportion of cases of jaundice produced this agglutination. Such an occurrence makes it necessary to employ cultures of more than one strain for diagnostic purposes.

We feel that this is an additional argument in favour of the view we have previously expressed that " until some method of standardizing cultures of leptospira is employed, the serological diagnosis of Weil's disease should be undertaken only at laboratories where the idiosyncrasies of the antigens are well known."

We wish to express our thanks to Col. W. H. O'Riordan, *M.C.*, O.C. Cambridge Hospital, Aldershot, and to Lieut.-Col. N. T. Whitehead, *M.C.*, R.A.M.C., assistant director of pathology, South-Eastern Command, for placing every facility at our disposal during this investigation.

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SYMPTOMATOLOGY OF MALARIA

BY

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Since April, 1942, I have been medical officer to a unit heavily exposed to malaria. During the hot months we had many cases of acute febrile malaria, 80% of which were malignant tertian infections. Hyperpyrexial, cerebral, and bilious forms were encountered, and one quickly grew accustomed to the vagaries and complications of malaria in its acute forms, and later to the so-called chronic malaria with its enlarged spleen, anaemia, and general ill-health.

With the onset of the cold weather fresh cases rapidly diminished, although I was faced with a large number of patients with relatively trivial complaints whom I at first treated on conservative orthodox lines according to their symptoms, but with no success. Headaches and pains in the back were evidently not English aches and pains. Dismissing the possibility of malingering by reason of my personal knowledge of the patients, I remembered that the largest pathological factor in this part of India was malaria, and, having access to a microscope, I began a general investigation of all cases reporting sick.

I hope, by recording the following cases, to show that malaria is something more than an acute febrile disease, and that it can produce such varied symptoms as pains in the back, rheumatic pains about joints, pains in the testicles, urticaria, multiple conjunctival ecchymosis, cardiac irregularity, recurrent diarrhoea, and obstinate eczematoid conditions without fever. I cannot say dogmatically that these symptoms and malaria are direct cause and effect, but I suggest that there is weighty evidence in favour of this, having regard to the positive blood examinations and the results of treatment.

Case Records

Case 1.—Complained of severe pain in the back, worse at rest than when walking about; no history of malaria; treated for several days as lumbago with liniment and mist. sod. sal. without improvement. A thick blood film showed B.T. rings and trophozoites; the spleen was not palpable though the splenic area was dull to percussion. A standard course was given and all symptoms disappeared on the third day of treatment.

Case 2.—He had severe pain over second costal cartilage on left side. This appeared swollen and was tender on pressure. There was also clinical evidence of anaemia and general ill-health. A thick blood film revealed M.T. rings; the spleen was not palpable. After a course of standard treatment all symptoms disappeared.

Case 3.—This patient had severe pain in left side of chest over fifth, sixth, and seventh ribs, worse on breathing. There was no fever and no physical sign in the chest. The tip of the spleen was palpable, and a thick film revealed M.T. rings and crescents. All symptoms subsided after a standard course.

Case 4.—Complained of recurrent swellings of the face; there was no history of any previous allergic phenomena. A blood slide revealed B.T. rings and trophozoites. After a standard course no further swellings occurred. A previous similar case had been seen in a patient with recurrent benign tertian malaria. This man had urticarial swellings of face and over both tibiae and above the ankle-joint. A third case showing B.T. rings has also been seen.

Case 5.—He developed a patch of dry scaly eczema with occasional formation of vesicles and pustules just above the left knee; other less-marked but recurring areas of dry scaling with erythema were apparent on the flexor aspects of the arms. Exposure to sun aggravated the condition. The spleen was not palpable, but thick

blood film showed M.T. rings and crescents. There was evidence of anaemia. After a standard course the patches of eczema subsided for the first time over a period of three months.

Case 6.—He had clinical malaria four months previously and showed a large conjunctival ecchymosis. B.T. rings and trophozoites were found in thick film. No fever was present. Acute conjunctivitis with enlarged superficial blood vessels has also been seen which failed to respond to treatment on orthodox lines. M.T. parasites were found in thick blood film. The condition cleared after standard treatment. A third similar case of this type cleared very slowly under silver nitrate drops. Later, B.T. rings were found in the peripheral blood.

Case 7.—Complained of palpitation, and on examination a gross irregularity of pulse was found with dropped beats corresponding to extrasystoles, heard on auscultation of the heart. The irregularity disappeared on exercise. Thick blood film showed B.T. rings. After rest and standard treatment no further irregularity was detected. The spleen was not palpable.

Case 8.—Had pain in the left shoulder, slight pain in the right shoulder and left hip. There was low fever, 99° to 100°; the pulse rate was 120 standing and 90 lying. An apical systolic murmur was heard. A diagnosis of rheumatic fever was made, but a thick blood film showed M.T. rings. After a standard course he was restored to normal health.

Case 9.—Complained of pain and swelling in testicle. Right testicle swollen and acutely tender on palpation. Low fever 99° to 100°, headache, and malaise. A blood slide revealed M.T. rings and crescents. A standard course was given and the symptoms subsided rapidly. On rectal examination prostate normal; prostatic massage yielded only a little clear fluid; vesicles not palpable.

Case 10.—This is one case of many which showed identical symptoms—i.e., profound lassitude, frontal headache, and loss of appetite. No previous history of malaria. Thick blood film showed M.T. rings and crescents. There was evidence of anaemia. A standard course restored him to normal health.

Case 11.—Another example of several similar cases. Acute diarrhoea responding to intestinal sedatives but relapsing immediately these were withdrawn. There was loss of weight and appetite. Examination of the stools produced no microscopical evidence of disease. A thick blood film showed M.T. rings, and the diarrhoea responded to standard treatment.

Discussion

These cases suggest that the malarial parasite can exist in the peripheral blood and produce diverse pathological conditions without pyrexia.

The efficacy of treating a whole unit with antimalarial drugs —e.g., blanket treating—has been known for a long time, but with a supply of drugs that is not unlimited this is wasteful. Instead of indiscriminate "blanketing" it would be better to treat selectively, choosing any man obviously below normal health, where possible checking each case by thick blood preparations. It is a shibboleth that parasites cannot be found except in febrile cases. M.T. rings and B.T. trophozoites and rings can be found if the same diligence is used in searching a thick film as is necessary in thin films. The crescent, too, can be seen, though it is often too distorted for confident diagnosis.

Manson-Bahr describes a physical sign which I have found most useful as confirmatory evidence of malaria. In health the conjunctival blood vessels are few in number, pale-coloured, and of fine calibre; in other acute fevers they are often multiple and arranged radially, giving the eye a hazy pink appearance. In malarial infections, acute or afebrile, vessels of deep red colour and greater width can be seen winding a tortuous course on the surface of the conjunctiva. They are not especially numerous, nor is the whole of the conjunctiva necessarily involved. I have seen an extensive ecchymosis spread from one of these vessels during acute febrile malaria. If this can happen here it is probable that it can happen on any mucous membrane or indeed in any part of the body, and it offers an explanation of many of the obscure symptoms that may be encountered, such as the common throbbing frontal headache.

I submit that our conception of malaria as an acute fever is only one half of the truth and that it is also a generalized disease of arterioles and capillaries capable of producing a multitude of symptoms relative to the state and site of these vessels without any accompanying fever.

My acknowledgments are due to Brigadier McLeevey, who kindly read and approved this paper for publication.

GAS INFECTION OF THE BRAIN AS ONE FORM OF THE SERIOUS COMPLICATIONS OF CEREBRO-CRANIAL INJURIES

REPORT BY A COMMITTEE OF SOVIET SCIENTISTS (162)*

It is sometimes difficult to explain the various forms of serious complications arising from cerebro-cranial injuries. Very often these injuries run a different course in respect of the onset of granulation, conclusion of healing, and types of complications, in spite of the fact that they have the same localization, the force damaging the cranium is the same, and the missile is similar. The whole series of acute meningo-encephalitic complications which occur in the first stage of evacuation, in the F.M.H. (Field Mobile Hospital) of the first and second lines, attract attention and demand explanation.

It is now generally accepted that injuries sustained in the present war, including cerebro-cranial ones, are mostly infected. The range of pathogenic organisms infecting the wounds is very large. Gunshot and explosive missiles are in the majority of cases causing badly lacerated, contaminated, and consequently infected wounds. Data collected by Soviet authors and published during the civil war proved that the majority of cerebro-cranial injuries were caused by shell fragments, mines, etc.—not bullets—resulting in blind tracks, with retained pieces of clothing, dirty hairs, etc. Bullet wounds, particularly penetrating ones, were in the minority.

The Infective Organisms

We undertook investigations with the consent and support of the Chief Military Medical Directorate of the Red Army. We carried out intensive and detailed bacteriological examination of cases of cerebro-cranial injuries, and came to the conclusion that they were infected with the same micro-organisms as muscular injuries. Sterile wounds were rare: from 300 cases only 2 were registered as sterile. Of cases of cerebro-cranial injuries 61.7% were infected with cocci (*Streptococcus anaerobius, Str. pyogenes longissimus, Str. pyogenes longus, Str. brevis, Staph. pyogenes aureus, Staph. pyogenes albus,* micrococcus, diplococcus, *Gaffkya tetragena,* etc.).

Of our cases 20.5% were infected with putrefactive aerobes (*Bact. megatherium, Bact. mycoides, Bact. mesentericus, Bact. subtilis, Proteus vulgaris, Kurthia zenkeri*). 11.2% were caused by gas-producing anaerobic organisms, the great majority (94%) being *Cl. perfringens*; next came *Cl. oedematiens* (12.1%) —in only one case was there *Cl. oedematis maligni.* 6.2% were caused by putrefactive anaerobes—*Cl. sporogenes, Cl. putrificum, Cl. butyricum,* and *Cl. tetanomorphum. Cl. perfringens* is usually found in cerebro-cranial injuries in combination with putrefactive anaerobes, aerobes, and streptococci.

Table I gives comparative percentages of various organisms in cases treated in the F.M.H. during 1½ months after the injury; in cases transferred from other hospitals 1½ to 2 months after the injury and treated in the neurosurgical clinic of the Institute of Experimental Medicine; and cases treated in the Institute of Experimental Medicine 1 to 1½ months after the injury and receiving a course of sulphonamide therapy.

TABLE I.—*Percentages of Various Organisms*

	F.M.H.	Neurosurg. Clinic	Sulphonamide Therapy
Pathogenic anaerobes ..	13%	6%	9%
Putrefactive anaerobes ..	15·5%	18·3%	2·6%
Putrefactive aerobes	38%	50%	13·1%
Pathogenic streptococci ..	35%	41%	7·9%
Various cocci	75·52%	80%	94·7%

The figures in the table show that the more serious types of infection are met with during the first few days; later some of the patients die, and in some the pathogenic organisms disappear and are replaced by non-pathogenic ones (cocci). In neglected wounds the percentage of putrefactive organisms

* Translated by A. Fry, M.R.C.S.

increases. The local use of sulphonamides accelerates the process of clearing the wound of pathogenic organisms.

The part played by infection in penetrating wounds of the skull is very great, as the percentage of fatal results with anaerobic infection (gas gangrene) is high (Table II).

TABLE II.—*Percentages of Fatal Results*

Type of Infection	All Cases	Cases in F.M.H.
Pathogenic anaerobes	33%	50%
Putrefactive anaerobes	16%	15·4%
Putrefactive aerobes	6·5%	12·8%
Cocci	0·4%	1·5%

Although the general mortality due to coccal infection is the lowest it differs for various cocci: the most pathogenic are *Str. pyogenes longissimus* and *longus*; the mortality due to these in the F.M.H. is 3.1%, whereas the percentage of fatal cases due to all the other cocci is *nil*.

The healing process is also influenced by the type of infection in a way similar to Table II. Two cases with sterile wounds had healthy granulations on the eighth day, and scarring began on the eighteenth day in spite of the depth of the cerebral damage (5 cm. and 8 cm.). In 14 cases of penetrating and non-penetrating cranial injuries infected with staphylococci and micrococci the wounds were sterile about a month after the injury. Of 12 cases of infected non-penetrating cranial injuries 7 were sterile in the same period. Of 20 infected penetrating cranial injuries only 2 were sterile. Putrefactive aerobic infection gave sterile wounds in 4 out of 16 when the dura mater was not damaged, and 2 out of 16 when the injury was a penetrating one.

Of the greatest interest for us were the cranial injuries infected with spore-forming organisms (anaerobes). The clinical course of such cases varies, and there are four different forms: (1) acute; (2) subacute, 1 to 2 months; (3) chronic, 2 to 4 months; (4) latent. The last form comprises those cases which have a favourable clinical picture but in which pathogenic anaerobes continue to be isolated from the wound. We had 6 such cases, and in 2 we found *Cl. perfringens*, which was lethal for certain animals (white mice).

Table III gives the mortality and the favourable results of gas-gangrene-infected cases in the four clinical forms.

TABLE III

	Acute	Subacute	Chronic	Latent
Total cases	10	9	14	6
Died	8	4	5	0
Favourable result ..	2	5	9	6

Cultures taken from heart, liver, spleen, wound, etc., 10 to 24 hours after death have grown *Cl. perfringens* pure or in combination with *Cl. sporogenes*, *Cl. putrificum*, and *Cl. oedematiens*. Cultures grown post mortem have shown the presence of the same micro-organisms as during life. All facts proved that the cerebro-cranial wounds were the source of sepsis. All tests for the virulence of infection were performed on white mice weighing 40 to 50 g.; the culture used was 18 to 20 hours old, and the dose 0.3 c.cm. by intramuscular route into the thigh. The organism was afterwards verified post mortem from the animals' organs by growing it on Wilson and Blair's medium.

The high percentage of deaths from pathogenic anaerobic infection of cranial wounds proves the great virulence of the organisms. In the 39 cases of anaerobic cerebral infection there were found:

Cl. perfringens	in 36 cases	Cl. tetanomorphum	in 12 cases
,, oedematiens	,, 4 ,,	,, butyricum	,, 11 ,,
,, sporogenes	,, 15 ,,	,, tertium	,, 1 case
,, putrificum	,, 13 ,,		

The clinical picture of infection of the brain by gas-forming anaerobes is characterized by the following signs and symptoms: (1) gas gangrene; (2) discharge of necrotic brain tissue and debris from the wound; (3) colourless, watery, purulent discharge; (4) acute and putrid smell of the wound; (5) formation of gas in the wound; (6) oedema; (7) prolapse; (8) meningitis; (9) low temperature with rapid pulse; (10) abscesses; (11) severe "bursting" headaches; (12) blood picture (increase in number of lymphocytes and high sedimentation rate); (13) nausea and vomiting; (14) depressed state of patient; (15) general appearance; (16) delay in formation of granulation.

In the acute form we find: gas gangrene, discharge of necrotic brain tissue and debris, gas formation in the wound, acute and putrid odour, oedema, prolapse, severe bursting headaches, frequent septic complication, and death. In the subacute and chronic forms there is first of all gas formation in the wound; then watery discharge, acute and putrid odour, oedema, prolapse, and gangrene; later, sometimes after the external healing of the wound and apparent cure, there appear metastatic abscesses of anaerobic aetiology and meningitis, followed in some cases by death. In the latent form, to which belong all carriers—particularly of *Cl. perfringens*—there is a slow progress of wound-healing without the characteristic symptoms of gas-anaerobe infection.

In view of the fact that the carrier rate of gas-infection micro-organisms was found to be 11.2% in cases of penetrating injuries of the skull, the majority of which resulted in gangrene, it is obvious that this affection is very common. Our most important, and vital, task is therefore to lower the mortality rate of gas gangrene, and the means to achieve it are as follows:

1. The use of prophylactic anti-gas-gangrene serum in doses of 5,000 to 10,000 units.

2. The timely use of sulphonamides—locally and as an emulsion in castor oil or cod-liver oil (10 g. sulphanilamide, 10 g. sulphathiazole, in 80 to 100 c.cm. of castor oil); sulphathiazole orally 6 g. daily for 6 days; intravenously, 1% solution of sulphathiazole 30 to 40 c.cm. two to three times in 24 hours.

The facts about the action of sulphonamide emulsion will be discussed in a separate article.

For the better illustration of our suggestions about the conduct and treatment of gas infection of the brain we append abstracts of some of our cases.

Acute Form (Gas Gangrene of Brain)

Cases Ending Fatally

Case 1.—Wounded March 15, 1942; died March 23. There was a transverse wound in the right temporal bone 4 by 9 cm.; brain tissue was protruding from the wound, which was partly gangrenous and had an offensive odour. On the day of death the following signs and symptoms were noted: general state grave; unconscious; some dark-red brain matter was discharging and some gas bubbles were apparent in the wound. Necropsy showed considerable gangrene of the temporal region of the brain. Bacteriological findings in the wound and at necropsy were *Cl. perfringens* and *Cl. sporogenes*.

Case 2.—Wounded March 7, 1942; died March 31. An extensive brain lesion was found on trephining. The brain and dura mater were pulped and there was about 5 c.cm. of brain debris. Offensive odour. Grave condition of patient. Necropsy: semifluid mass with debris in the posterior part of the right cerebral hemisphere, with sero-purulent fluid and offensive smell. On section the cerebral cortex showed considerable loss of definition. Bacteriology: From wound while patient was alive—*Cl. perfringens* and *Staph. pyogenes longus*; at necropsy—the heart, liver, and spleen contained *Cl. perfringens*, the pathogenicity of which was confirmed on animal inoculation.

Case 3.—Wounded March 3, 1942; died March 7. Bone fragments, pieces of cap, and skin with hair were extracted from the depth of the brain wound, which was 7 cm. long. The discharge was dirty and purulent, and consisted of necrotic cerebral tissue with an offensive odour and gas bubbles. Condition grave; bursting headache; unconsciousness Necropsy showed extensive gangrene of brain tissue and loss of cortical definition. Bacteriology: From wound discharge—*Cl. perfringens, Cl. sporogenes, Cl. butyricum, Bact. mycoides, Proteus vulgaris*; at necropsy—*Cl. perfringens* and *Cl. sporogenes*.

Cases with Favourable Issue

Case 4.—Wounded April 3, 1942; a cranial bony defect 1 by 1 cm. was found during operation, with herniation of cerebral matter. A cavity was present in the temporal lobe from which gas escaped with a whistling sound and about 10 to 12 cm. of brain debris with purulent odour. The cavity was packed with emulsion of sulphanilamide and sulphathiazole. Condition grave; severe headache. Bacteriology: *Cl. perfringens, Cl. sporogenes, Cl. putrificum, Str. pyogenes longus*. April 3: On removal of the packing there was a sharp purulent odour. April 8: Absence of cerebral pulsation. April 11: Cerebrospinal fluid appeared from the wound. The emulsion of sulphanilamide and sulphathiazole in castor oil was applied on April 8, 11, 15, 20, and 23. The general state of the patient improved

considerably during that period; the formation of gas in the wound stopped; the prolapse of brain tissue disappeared together with the sero-purulent discharge; granulation began. Bacteriology: *Cl. perfringens* isolated on April 12. On April 20 no more were seen. The culture of the organisms from the wound proved very virulent to animals. The patient was under observation until July 15, when he was discharged from our clinic.

Case 5.—Wounded on March 11, 1942. He was operated on on March 20, being in a very serious condition. There was a cranial defect between the parietal bones from which gangrenous portions of the brain and free bony fragments were protruding. The lesion was 6 cm. deep. There was about 15 c.cm. of putrid discharge with brain debris. The cavity was packed with our compound emulsion. March 23: Oedema of soft tissues of scalp; right-sided paresis and unconsciousness. Bacteriology during March 22 to 30: *Cl. perfringens, Cl. butyricum, Str. pyogenes.* Locally, sulphanilamide and sulphathiazole emulsion in castor oil was applied on March 23, 26, 30, April 3, 6, and every third day afterwards; orally, sulphathiazole, 4 doses of 1 g. on March 21, 22, 23, 24, 25, and 26. On March 26 the characteristic symptoms and signs of gas infection ceased. The patient's condition remained serious till April 5. April 9: Considerable improvement in patient's general condition: lively cerebral pulsation, granulation, amount of purulent discharge considerably lessened. Cultures from the wound on April 12 and 15 showed absence of *Cl. perfringens.* Patient remained in the clinic till April 20, when he was evacuated in good condition to the base hospital. Cultures of *Cl. perfringens* from the wound proved very virulent to animals. The rapid change in improvement in favourable cases is very characteristic of the acute form of gas infection (gas gangrene of the brain).

Subacute Form

Cases with Fatal Result

Case 6.—Wounded Feb. 22, 1942; died April 27. At the operation performed by us on March 12 at the F.M.H. we found, on enlarging the bony defect in the skull, a necrotic region of the brain and tracks in the frontal direction 7 cm. and in the occipital direction 4 cm. long. A dirty-coloured fluid with brain debris of offensive odour was found in those cavities. Cultures showed *Cl. perfringens.* An emulsion of 1 part of sulphanilamide and 2 parts of sulphathiazole was used locally throughout. General condition of patient grave; prolapse of cerebral matter; bursting headache; semiconsciousness; offensive sero-purulent discharge; later meningitis; at the end progressive cerebral abscess. At necropsy *Cl. perfringens* was found in the cerebral abscess and various organs.

Case 7.—Wounded March 3, 1942; died April 6. Muscular rigidity in the beginning; copious discharge; prolapse of brain tissue; bursting headache. Compound emulsion used throughout. Bacteriology (March 10): *Cl. perfringens, Bact. megatherium, Kurthia zenkeri,* streptococci. Signs of cerebral abscess appeared at the end of March. *Cl. perfringens* was isolated post mortem.

Case 8.—Wounded March 6, 1942; died May 4. Prolapse of cerebral tissues; gas bubbles; penetrating wound of left parietal region with necrosis of temporo-parietal cerebral regions; *Cl. oedematiens, Cl. sporogenes, Cl. putrificum.*

Chronic Forms

Fatal Cases

Case 9.—Wounded Dec. 21, 1941; died April 29, 1942. Diagnosis: penetrating wound of right temporal region. Condition during the prolonged period—serious. Operation was performed on Jan. 23. Fragments extracted from the cerebral wound. Subsequently there was a profuse offensive purulent discharge; meningeal symptoms; neck rigidity. Bacteriology (Feb. 2): *Cl. oedematiens, Cl. perfringens,* staphylococci, streptococci, *Proteus vulgaris.* Local application since Feb. 3: sulphanilamide and sulphathiazole 1:2 in vaseline oil; sulphanilamide solution intravenously; orally, sulphathiazole 1 g. six times daily for 5 days. Condition on Feb. 6 satisfactory; on Feb. 10, good. On Feb. 13, 17, 26, and March 19 no micro-organisms were found. On March 3 granulation started. However, towards the end of April symptoms of progressive cerebral abscess began, accompanied by meningitis, and on April 29 the patient died. Necropsy: Abscess in right temporal lobe; purulent meningitis. Bacteriology: *Cl. perfringens* from the abscess, blood, and spleen; *Cl. oedematiens.*

Case 10.—Wounded Jan. 23, 1942; died April 20. Until Feb. 15 Vishnevki's ointment was used. Feb. 15: Operation, when non-pulsating prolapse of brain was found. After excision of the prolapse, puncture of frontal and temporal lobes was performed, when pus with gas bubbles was obtained. A fistulous track covered with cerebral tissue was observed in the temporal direction. 20 c.cm. of pus was found. The wound was filled with 20% emulsion of sulphanilamide and sulphathiazole 1:2 in castor oil. The bursting headache improved after the operation. Bacteriology of discharge (Feb. 16 to March 3): *Cl. perfringens, Cl. putrificum, Cl. sporogenes, Cl. tetanomorphum, Cl. butyricum*; together with staphylococci, streptococci, *B. coli.* March 12: No more pathogenic micro-organisms. March 17: Wound sterile, with healthy granulation and little discharge. March 23: Good general condition. From the beginning of April, however, the condition got worse: severe headache, right facial paralysis, rigidity, positive Kernig sign. Cerebral abscess was diagnosed. Patient operated on again, but died from heart failure. Bacteriology of brain post mortem: *Cl. perfringens,* which, although it disappeared from the wound while the patient was alive, caused the cerebral abscess, which proved fatal.

Cases with Good Result

Case 11.—Wounded Nov. 27, 1941. Diagnosis: comminuted wound of skull penetrating the cranial cavity. Vishnevki's ointment was applied until Dec. 17. Dec. 17: Discharge of brain debris with profuse offensive purulent discharge. Jan. 22, 1942: Operation. Bacteriology: *Cl. perfringens, Cl. oedematiens.* From Feb. 25 anaerobes disappeared. Emulsion of sulphanilamide and sulphathiazole in castor oil was used locally from Feb. 9. March 7: Condition good; patient was then evacuated to a base hospital.

TABLE IV.—*Results of Experimental Work on Animals infected with Gas Gangrene of the Brain*

Experiment No.	Animal	Infection Route	Dose of Infection c.cm.	Infecting Organism	When Died	Cultures Obtained	Post-mortem Findings
1	Cat	Intracerebral	0·50	Cl. perfringens	18 hrs.	Heart: sterile	Encephalitis; haemorrhages
	Mouse 1	"	0·20	"	"	Cl. perfringens	Acute encephalitis; oedema; cerebral softening
	" 2	"	0·20	"	"	"	" " " "
	" 3	"	0·20	"	"	"	" " " "
	" 4	"	0·20	"	"	"	" " " "
	" 5	"	Sterile bouillon 0·50	—	Alive; killed	Sterile	—
2	Rat 1	"	0·05	Cl. perfringens	18 hrs.	Heart: Cl perfr.	Cerebral oedema
	" 2	"	0·05	"	"	" "	" "
	" 3	"	0·10	"	"	" "	" "
	" 4	"	0·10	"	"	" "	" "
	" 5	"	0·50	"	Alive	" "	—
	" 6	Thigh muscle	0·05	"	"	—	—
	" 7	"	0·10	"	"	—	—
	" 8	"	0·10	"	"	—	—
	" 9	Intracerebral	0·10	Str. pyogenes	48 hrs.	Heart: Strep.	Picture of general sepsis
	" 10	"	0·10	"	"	" "	" " "
3	Rat 1	"	0·01	Cl. perfringens	18 hrs.	Cl. perfringens	Cerebral softening
	" 2	"	0·01	"	"	"	"
	" 3	"	0·02	"	20 hrs.	Heart: Cl. perfr.	Cerebral oedema; pulmonary haemorrhages
	" 4	"	0·02	"	"	" "	"
	" 5	"	0·02	"	18 hrs.	" "	Cerebral oedema and softening; pulmonary haemorrhages
	" 6	"	0·05	"	"	" "	"
	" 7	"	0·10	"	"	" "	Oedema and cerebral haemorrhages; pulmonary haemorrhages
	" 8	"	0·10	"	24 hrs.	" "	Lungs: hepatinization and haemorrhages
	" 9	"	0·20	"	—	—	" "
	" 10	Thigh muscle	0·10	"	—	—	Severe oedema of thigh
	" 11	" "	0·10	"	—	—	Oedema of thigh
	" 12	" "	0·50	"	—	—	Severe oedema of thigh and abdomen
	" 13	Intracerebral	0·01	Sterile bouillon	—	—	—
	" 14	"	0·05				
	" 15	"	0·05				

Case 12.—Wounded Dec. 1, 1941. Diagnosis: penetrating comminuted wound of temporal region of skull. Vishnevki's ointment applied till Feb. 10; from Feb. 10 sulphanilamide and sulphathiazole. Condition: December, serious; January, less serious; from Feb. 14 patient felt much better. In March, evacuation to the base. Bacteriology on Feb. 4 showed *Cl. perfringens*. No pathogenic organisms after Feb. 13.

It is evident, in the subacute and chronic forms of anaerobic infection of the brain, that if the disease progresses without metastases (cerebral abscess) the prognosis is good; but if metastases of anaerobic origin appear the result is serious.

Case 13.—Wounded Dec. 24, 1941. Feb. 18, 1942: Operation; intracerebral abscess found, cavity 6 cm. deep. Bacteriology (Feb. 18, 24, March 3, 16, 26, 31): *Cl. perfringens* virulent to animals tested March 23. Culture on April 11 was already less virulent. In spite of the findings the general state began to improve after March 30. Granulations appeared on March 3.

Discussion

It is obvious that the symptoms and signs of gas gangrene of the brain in all its forms depend on several causes—virulence of the anaerobe, type of trauma or crushing of cerebral tissue, degree and depth of infected wound, disturbance of circulation, resistance of patient, etc. Gas infection of the brain has several distinguishing signs and symptoms as compared with the similar infection of muscles—prolapse of cerebral tissue, bursting headache, meningitis, absence of crepitations (as in muscles).

Prof. Sacharov is carrying out experimental work on rats and mice infected with gas gangrene of the brain (Table IV). Infecting the animals with *Cl. perfringens* directly into the cerebral hemispheres beneath the dura mater without causing any trauma to the cerebral tissue, he was able to demonstrate that they died from acute cerebral oedema, cerebral softening, and other septic symptoms of gas infection.

Several cases of cerebral abscesses of anaerobic origin have been described: during the war of 1914-17 Academician Burdenko observed cerebral abscesses containing anaerobes. There has, however, been no research into gas infection of the brain complicating cerebro-cranial injuries. Military Surgeon Frantz gives statistics of 118 cases of gas oedema of the brain during the war of 1914-17; but his data are incomplete, as they do not include anything of clinical or bacteriological value.

Conclusion

Our experience proves that the best results in gas infection of the brain are obtained by active surgical intervention and the use of anti-gas-gangrene serum. We boldly dealt with the excision of prolapsed brain tissue, the gas infection, and the removal of necrotic tissue, applying sulphanilamide and sulphathiazole emulsion to the cavity. Orally we gave sulphanilamide 1 g. six times in 24 hours; and, intravenously, 1% solution of sulphathiazole 2 to 3 times daily in doses of 30 to 40 c.cm. in meningeal involvement, with 0.8 g. sulphanilamide intrathecally. We carefully watched the blood for any signs of agranulocytosis. Where this occurred we gave a blood transfusion and did not stop the active sulphonamide therapy. But very often in such a complication we reduced the sulphonamide dose, and in order to lessen the toxic effects on the blood transfused 250 to 350 c.cm. of blood, using anti-gas-gangrene serum at the same time. In our opinion it is imperative that instruction should be issued to all front-line dressing stations about the use of anti-gas-gangrene sera and local and oral sulphonamide therapy in contaminated penetrating cranial injuries, which are so often complicated by gas gangrene.

The Interdepartmental Committee on Dentistry, recently set up under the chairmanship of Lord Teviot by the Minister of Health and the Secretary of State for Scotland, has invited certain interested bodies, including associations of local authorities and dental associations, to submit evidence bearing on their terms of reference, which are as follows: To consider and report upon (*a*) the progressive stages by which, having regard to the number of practising dentists, provision for an adequate and satisfactory dental service should be made available for the population; (*b*) the measures to be taken to secure an adequate number of entrants to the dental profession; (*c*) existing legislation dealing with the practice of dentistry and the government of the dental profession; (*e*) measures for the encouragement and co-ordination of research into the causation, prevention, and treatment of dental diseases.

Medical Memoranda

Trophic Necrosis, Skin-grafting, and Vitamin C

During 20 years' practice I have seen 3 cases of scurvy, all within the last four years. There are now simple methods of estimating vitamin excretion in the urine applicable directly to ascorbic acid, thiamin hydrochloride, and nicotinic acid, and indirectly to vitamins A and D. Soon riboflavin is likely to join the former category. It is therefore possible to approach the subject of avitaminosis without dependence on theoretical and commercial claims, and to do so is to learn much of interest and value. This is illustrated by the two undermentioned cases of ulceration of the leg.

CASE I

A farmer's widow aged 69 complained of sores on the leg. Onset was acute, with much pain. She was of a thin hard-working type. Temperature 100°. Three areas of discoloration and apparently superficial ulceration on the right leg. Large varicose veins. Urine contained neither sugar nor albumin. W.R. was negative. Two days later the three ulcers had become circumscribed patches of black moist gangrene. She was removed to hospital. Fresh ulcers appeared, and she developed circumcorneal ulceration. There was no improvement until, on finding that the urine contained no ascorbic acid, 150 mg. of ascorbic acid was given daily by the mouth. Skin-grafting of the two largest patches, 3 in. by 2 in., was successful, and progress was uninterrupted.

CASE II

A woman aged 70 has for 20 years had large superficial areas of ulceration of both legs, 4 in. by 6 in., and extending halfway round the limbs. There were no visible varicose veins. The skin generally was thin and white. Five years previously this patient was in hospital under my care. Routine treatment was without effect and skin-grafting completely failed.

She was readmitted on Aug. 2, 1942. No vitamin C (ascorbic acid) excreted in the urine. Course of ascorbic acid, 150 mg. daily, begun. First leg grafted Aug. 9 (Reverdin); second leg grafted Aug. 31. Discharged healed, and much improved in general health, on Oct. 21.

COMMENT

These two patients illustrate another aspect of avitaminosis which I cannot at present explain—namely, the considerable individual variation in vitamin C sub-saturation found in practice. Case I required 150 mg. daily for 8 weeks before ascorbic acid was excreted regularly in the urine. On two occasions increase of the daily dose to 700 mg. secured small urinary excretion (0.8 and 1.5 mg. per 100 c.cm. respectively). Although this patient had achlorhydria (as is the rule when the urinary execretion of ascorbic acid is *nil*) the administration of HCl apparently did not improve the absorption of the ascorbic acid. Case II, on the other hand, showed urinary excretion of 1 mg. per 100 c.cm. on the sixteenth day, and maintained this rate.

The analyses were made by Mr. R. O. Eames, F.I.C.

The conclusion reached is that vitamin C is indicated in some cases of trophic ulceration, especially before skin-grafting, and the amount for control by estimation of the urinary excretion.

Caernarvon. GRIFFITH EVANS, F.R.C.S.

The Diagnosis of Alkaptonuria

Alkaptonuria is a rare irregularity. The symptoms are slight dysuria and frequency of micturition at night. The condition is said to be due to an inborn error of metabolism of the tyrosine linkage in the process of protein metabolism, the end-product being 1 : 4-dihydroxyphenyl-acetic (homogentisic) acid, which is passed into the urine. Alkapton urine is normal in colour when freshly passed, but on exposure to air and light rapidly darkens from the surface downwards, ultimately assuming a dark-brown or black colour. Addition of alkali increases the rate of oxidation. It reduces cupric oxide and also silver nitrate solution (cold).

1 : 4-dihydroxyphenyl-acetic acid may be regarded as a derivative of hydroquinone (Fishberg, 1942). Therefore its presence can be detected in urine quite readily by first making the urine strongly alkaline with caustic soda or caustic potash. A drop of the urine so treated will, when placed upon regulation sensitized photographic paper, instantly turn the latter black. This colour change does not take place with the substances occurring normally in urine, or pathologically except with homogentisic acid. Thus the diagnosis of alkaptonuria may be made.

School of Medicine, Royal Colleges, Edinburgh. J. NOËL GOULD. TUDUR GLYN THOMAS.

REFERENCE

Fishberg, E. H. (1942). *J. Amer. med. Ass.*, **119**, 882.

Reviews

UROLOGY IN WAR

Urology in War. Wounds and Other Emergencies of the Genito-Urinary Organs, Surgical and Medical. By Charles Y. Bidgood, Lieut.-Commander, U.S.N.R., Chief Urologist, U.S. Naval Hospital, Washington. ($2.00 or 11s.) Baltimore: The Williams and Wilkins Company; London: Baillière, Tindall and Cox. 1942.

This small handbook of 78 pages will be useful as a manual of reference to those engaged in the general surgery which war inevitably provides. In wartime high specialization is only a make-believe. Bombs and bullets do not respect anatomical limitation: the injuries are usually multiple and widespread. The scope of the book is made clear in a foreword by Rear-Admiral McIntire, Surgeon-General U.S. Navy. It is intended not necessarily for urologists but for surgeons who have to care for emergency conditions arising from wounds or disease of the genito-urinary tract. The surgeon on active service needs wide training in general surgery in order to fulfil his mission. He will welcome small volumes for his portable library such as that under review. If some wound of the genito-urinary tract calls for priority in treatment, he has at hand instructive information presented in attractive form. In an emergency he will gain rapid guidance from 27 descriptive and elegant illustrations.

Ruptured urethra is a comparatively common injury in war. The recommendations for treatment lack clarity and are too short. Fig. 10 illustrates the operation for anastomosis of the urethra described and illustrated by W. de C. Wheeler (*Proc. roy. Soc. Med.*, 1928-9, **22**, 469). Other sections give treatment in more detail and sometimes with an exactitude which leaves nothing to be desired. Some novel procedures are illustrated, such as the transfusion of blood into the corpus cavernosum, when the veins of the limbs are not available.

A SYNOPSIS OF TROPICAL MEDICINE

Synopsis of Tropical Medicine. By Sir Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P. (Pp. 224; with 5 plates. 7s. 6d.) London: Cassell and Co., Ltd. 1943.

Those who are familiar with *Manson's Tropical Diseases* will not fail to recognize the close connexion it has with the *Synopsis of Tropical Medicine*—in fact, the latter, by the same author, is a synopsis of the former. As the larger book deals with nearly every aspect of tropical medicine, so also does the smaller synopsis, the difference being largely due to the suppression of all redundant matter. The result is that the synopsis gives essentially the same information as the larger book but in a form which is more that of a catalogue and which, in consequence, is perhaps more difficult to read. Nevertheless the *Synopsis of Tropical Medicine* is a veritable mine of information which for all practical purposes is remarkably accurate and cannot fail to supply the student with all that he may require for the practice of medicine in the Tropics. The size of the book is such that it will slip into the jacket pocket, so that we predict it will be the constant companion of the very many whose duty it is, particularly at the present time, to practise in a field of medicine which in ordinary circumstances would have been closed to them. The author is to be congratulated on his very successful contribution to the war effort.

OTO-RHINO-LARYNGOLOGY IN THE SERVICES

The Ear, Nose and Throat in the Services. By R. Scott Stevenson, M.D., F.R.C.S.Ed., Major, R.A.M.C. Oxford War Manuals. (Pp. 116. 5s.) London: Oxford University Press. 1943.

The nature of the author's own service naturally makes him most familiar with practice in the Army, but he has designed his book to meet the needs of the Navy and the R.A.F. also. It will, however, be most useful to officers of the R.A.M.C. whose lot it is to deal with large numbers of minor maladies, especially of the ears, and a few serious cases. The author has put his knowledge and experience to good use in compiling this little manual, which is of necessity superficial, but in spite of its modest size contains a great quantity of information of the kind likely to be required. It recalls a similar book in French by Bourgeois and Sourdille which was most useful during the war of 1914-18, but since that time the electric otoscope, chemotherapy, and audiometry, besides other improvements, have come into general use, so that there is need for a modern book of the same type. The aim of practice in the R.A.M.C. is naturally to keep men fit for service, and if they need treatment to provide such treatment that the period of absence is as short as possible, the clinical material being drawn from a highly selected group of the population. Yet in spite of this process of selection the type of case which presents itself, having regard to the limitations of sex and age, differs but little from that encountered daily in departments for out-patients, and gross malingerers are quite uncommon—certainly much less common than the numerous neurotics who infest the civilian out-patient clinics to-day in their efforts to avoid some form of national service. This is an aspect of practice which total war has made almost universal. The author approaches with excellent sense the question of excising the tonsils in soldiers. It is an operation which is easily abused and is naturally rather discouraged, but where it is evident from the history that recurrent attacks of tonsillitis are making a man unfit and repeatedly absent, the man can easily be made fit and his health improved. If junior officers of the R.A.M.C. will read the book they will have reason to be grateful to Major Scott Stevenson for his guidance.

PAEDIATRICS

Advances in Pediatrics. Volume I. Editor, Adolph G. De Sanctis, M.D. (Pp. 306. 21s.) London: William Heinemann.

The 1942 Year Book of Pediatrics. Edited by Isaac A. Abt, M.D., with the collaboration of Arthur F. Abt, M.D. (Pp. 512; illustrated. 19s.) Chicago: The Year Book Publishers; London: H. K. Lewis and Co. 1943.

It is argued that the days of the textbook in medicine are past, for progress is too rapid, and large volumes taking a long while in preparation get out of date by the time of publication. There is certainly a lot to be said for this, especially in the postgraduate field, and the first volume of a new series entitled *Advances in Pediatrics*, edited by Dr. A. G. De Sanctis and consisting of a series of monographs, represents the new type of publication. Eleven authors have taken part, producing nine monographs and a final chapter on recent advances of a more miscellaneous type. Selection was guided by a questionary sent to the leading paediatricians in the United States, and the following are the titles of the subjects chosen as having shown important changes in the past two years: toxoplasmosis, virus diseases, chemotherapy, electro-encephalography, vitamin K, surgical treatment of persistent ductus arteriosus, prematurity, tuberculosis, endocrinology. Of these, the first can be mentioned for its novel character, the disease discussed being quite unknown in Great Britain; and for special merit Dr. Waldo E. Nelson's contribution on tuberculosis can be rightly singled out, although the whole standard is remarkably high.

In *The Year Book of Pediatrics* Profs. I. A. Abt and A. F. Abt continue their extremely able annual review of the literature, mainly American, in this field. As usual, the editorial comments form an important part of the book's value, and an excellent index makes it easy to use the volume as a work of reference. Among British authors cited it is a pleasure to see appreciation of Prof. C. McNeil's advocacy of infant hygiene and breast-feeding, and there are also various references to articles which have appeared in the *Archives of Disease in Childhood*. The illustrations are well chosen, and the standard of reproduction indicates that American editors and publishers have not yet had to grapple with paper shortage.

Notes on Books

In 1941 Mr. WILLIAM MAIR compiled *An Index of New Remedies* containing a list of recently introduced drugs, etc., with short notes on the therapeutic purposes for which they were recommended. In view of the desire of manufacturing firms to label their products with names registered as trade marks, and the hindrance that this is to the development of any rational nomenclature for new drugs, Mr. Mair's pamphlet provided a very useful work of reference. Its cordial reception in these columns and elsewhere has led to the preparation of a second series, *An Index of Modern Remedies*, which is published by the *Scottish Chemist* for the medical and pharmaceutical professions from 240, Albert Drive, Pollokshields, Glasgow,

at the price of 1s. 6d. Like the first, it is essentially an index. Information on any given item may be readily found by means of the alphabetical list at the end of the pamphlet.

The Metabolism of Fat, by IDA SMEDLEY-MACLEAN, D.Sc., of the biochemical department of the Lister Institute of Preventive Medicine, is a recent addition to Methuen's Monographs on Biological Subjects (price 5s.). It is an attempt to give in very brief compass a critical account of some of the more important developments in our knowledge of the metabolism of the fatty acids—a problem now being attacked by more and more investigators from widely different points of approach. For her present purpose the author has picked out what seemed to be the most significant results and has endeavoured to piece them together. The bibliography grouped under the several chapters will give useful pointers to those wishing to amplify this introduction to the subject by reference to contemporary periodical literature.

Preparations and Appliances

A PORTABLE SUCTION APPARATUS NOT DEPENDENT ON A SOURCE OF ELECTRICITY

N. F. SAHER, M.B., D.A., and R. SALT send the following description from the Nuffield Department of Anaesthetics, University of Oxford.

In the apparatus described here a cylinder of compressed gas, such as oxygen, is used as a source of energy. The gas is fed to an ejector unit and produces suction at any negative pressure up to a maximum of about 400 mm. Hg. When a cylinder containing 20 c.ft. of oxygen is used and the negative pressure is adjusted to 200 mm. Hg continuous suction can be obtained for about 40 minutes. Previously, suction apparatus working on the ejector principle was described by Mr. Norman Lake (1924). In his apparatus, however, the gas was fed direct from the cylinder to the jet of the ejector unit. While that arrangement was effective it was rather wasteful in gas, especially as the suction became practically ineffective as soon as the pressure in the cylinder fell below 30 atmospheres, which resulted in about a quarter of the contents of each cylinder being wasted. The apparatus now to be described is more efficient, and therefore more economical in gas: practically the whole contents of each cylinder can be used. Moreover, the negative pressure is easily adjustable.

The apparatus is built up on a stand, with castors, intended for an oxygen cylinder of either the 20-c.ft. or the 40-c.ft. size. To the cylinder is fitted a reducing valve (Fig. 1, A)—e.g., McKesson or similar type—having a tyre-clip adapter to which high-pressure tubing is attached. Through the tubing the gas is led to a Schraeder stop-valve (Fig. 1, C, and Fig. 2). This valve is placed in a convenient position to enable the oxygen flow to be switched on or off by foot control, which helps to economize in oxygen. When the foot button is pushed down, oxygen passes into the ejector system and produces a negative pressure at the entrainment port (Fig. 1, D, and Fig. 2). If the ejector is fitted with a No. 70 Amal jet it has been found possible to obtain any required negative pressure within the range mentioned simply by adjustment of the reducing valve, and at the same time to preserve a reasonable economy in oxygen consumption. A reduced-pressure gauge calibrated in mm. Hg (Fig 1, B) is provided on the low-pressure side, and indicates the negative pressure obtainable at various settings of the reducing valve. The outlet of the ejector system is fitted with a silencer (see Fig. 2). When the foot button is released the oxygen flow is stopped.

The entrainment port (Fig. 1, D) is connected by tubing to a glass bottle (Fig. 1, E), which is in a cage fixed to the cylinder stand. A second tube leads from the operation field. There, aspiration can be carried out with any of the various catheters or suction tips in common use. The aspirated material collects in the glass bottle.

Performance of the Apparatus

(*a*) *With the Reducing Valve set to 24 lb. per sq. in.*—The rate of oxygen usage is 12.5 litres per minute (measured at atmospheric pressure). When the suction side of the apparatus is closed to prevent entry of gas or liquid the negative pressure produced is 200 mm. Hg. As is to be expected, the time taken to attain this negative pressure depends upon the volume of air in the suction side of the system, mainly in the collecting bottle, before the oxygen flow is started, and upon the resistance of the tube connecting the ejector unit and the collecting bottle. This latter consists of two feet of thick-walled rubber tubing of 1/4 in. internal diameter. With an empty three-pint bottle the full negative pressure is attained in 11 seconds; with a one-pint bottle, in seven seconds. The rate at which the apparatus sucks up water through a Magill No. 0 tube, attached to the collecting bottle by a metal connector and four feet of thick-walled rubber tube of 1/4 in. internal diameter, is 1,200 c.cm. per minute. The rate at which the apparatus sucks up blood is about 1,020 c.cm. per minute. These figures give some idea of the capacity of the apparatus in the conditions stated. Naturally, the volume sucked per minute will be smaller if a fluid more viscous than blood is being dealt with. Moreover, if a longer tube is substituted for the Magill No. 0 or a tube of smaller bore is used, the resistance to the passage of fluid is higher and consequently the volume sucked per minute will be lower.

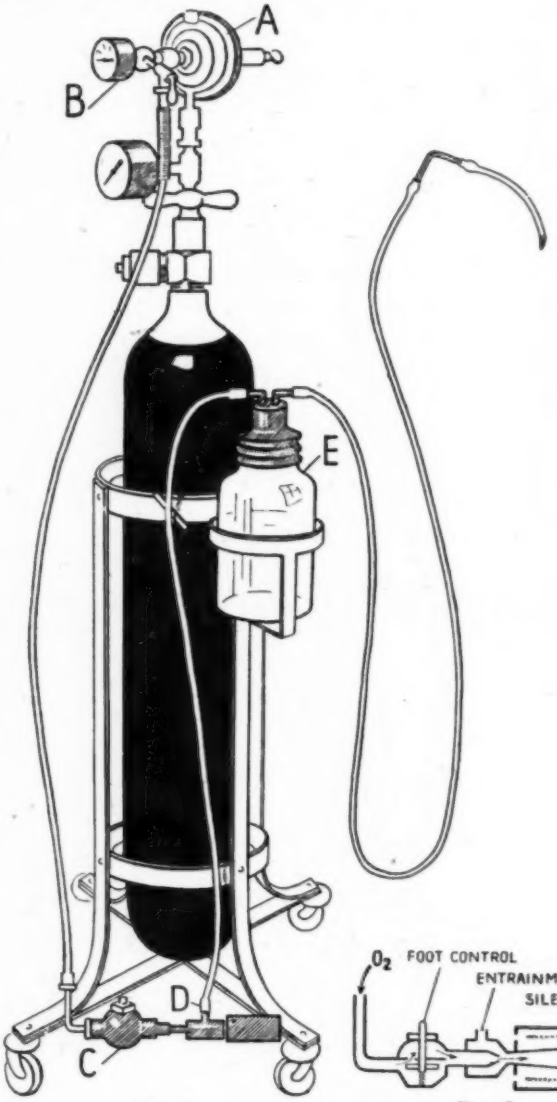

FIG. 1

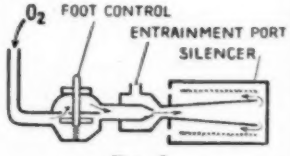

FIG. 2

As might be expected from the figures already given, the time lag between starting the oxygen flow and the beginning of suction flow is influenced by the size of the collecting bottle if empty, or the volume of the air space in the bottle if partly full. With a one-pint bottle the time lag before visible suction of water begins is about one second; with a three-pint bottle the lag is about 2½ seconds.

(*b*) *With the Reducing Valve set to 35 lb. per sq. in.*—The rate of oxygen usage is 15.5 litres per minute. The negative pressure produced when the suction side of the apparatus is closed is about 300 mm. Hg. Therefore a cylinder containing 20 c.ft. of oxygen provides continuous suction for about 30 minutes. The time taken to attain the full negative pressure of 300 mm. Hg is 15 seconds when an empty three-pint collecting bottle is used, and 11 seconds with a one-pint collecting bottle. Although there is a time lag before full negative pressure is reached, actual "entrainment" of water begins almost at once. The rate at which the apparatus aspirates water in the conditions stated above is 1,300 c.cm. per minute; for blood the rate is about 1,040 c.cm.

This apparatus can be obtained from Medical and Industrial Equipment Ltd. of 12, New Cavendish Street, London.

REFERENCE

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FOURTH CENTENARY OF "DE FABRICA"

This year marks the four-hundredth anniversary of an event of the highest significance for our civilization—the advent of the modern view of the material world. The universe of medieval thought was very different. In its centre lay the "corruptible" spherical earth. Round it circled in order the "incorruptible" heavenly bodies, each in its proper sphere and each sphere within the next, like skins of an onion. The influence of these bodies entered all earthly activity, disposing, if not forcing, even the human will. Hence the universal respect for astrology, which was a theory as to how the parts of Creation were related to each other. The world had been made for man, and it was natural to believe that his bodily organs were related to this plan, certain planets or constellations affecting certain organs. Thus arose elaborate schemes of the relation of the "Macrocosm"—the great outer celestial world—to the "Microcosm"—the little inner world of man himself.

In May, 1543, the aged Polish astronomer, Copernicus (1473-1543), lay on his death-bed and a copy of his book *On the Revolutions of the Celestial Spheres* was rushed to him. As all know, it sets the sun in the centre of the world and the earth, like other planets, moving round it, the whole system being bounded by an outermost starry firmament. This system was incompatible with medieval astrology and in that sense was revolutionary. Yet, despite the great battle that came to be fought in the name of Copernicus, it is not really a modern book in the proper sense. Its tone is still scholastic. It contains few observations. By retaining the system of regular movement in circles and the fixity of the firmament it proclaims its medieval roots. It is a work of ratiocination in the medieval manner. Utterly different was the other great scientific book of 1543, nor could two men be more contrasted than the Pole Copernicus and the Belgian Andreas Vesalius (1514-64), whose work is described on another page by Dr. E. Ashworth Underwood.

Vesalius studied at the Universities of Louvain and Paris. In both the teaching of anatomy was quite medieval in method and substance. The professor lectured always from his Chair, a physical reality in those days—a great pulpit with a reading desk. There he read from the text of Galen—hence the academic title "Reader"—commenting on it as he went, while his "Demonstrator" directed with his wand a menial to the actual task of dissection. All was done third-hand and according to the written word. Vesalius soon revolted against this system and betook himself to Padua, long renowned as a medical centre. By his work there he succeeded in a surprisingly short time in changing completely the whole content and tradition of thought about the human body, and indeed of thought about the universe as a whole. From his time we may date the establishment of anatomy as the positive basis of medical teaching. Vesalius was still only 28 when, in June, 1543, there was issued at Basle his *De humani corporis fabrica*. With this great book the scientific study of living things began again where Aristotle and Galen had left it in antiquity. The personality of Vesalius impressed itself on the whole conception of the human *fabrica*—a word which had, for him, the sense of something at work. It was always living anatomy that he was trying to describe, and, as a corollary, it was always the body as a whole that was in his mind. This vision of the living *fabrica* made him a great creative anatomist, but it made him at the same time a creative artist. Yet this vision makes his work difficult reading for us, since to understand it we must rid ourselves of certain ideas that we accept automatically and unconsciously. The modern biologist deals with descriptions and origins. He takes an organ or part or function or reaction or group of organisms, and investigates it in detail. Then he treats it comparatively and considers its relation and descent. His thought is always saturated with evolutionary implications. But with Vesalius it is not so. For him the body is a piece of living workmanship made by the Great Craftsman. The parts must be considered always in relation to the scheme as a whole, and treated as contributing to that complex that we call a man. Thus, for example, his famous general figures of bones or of muscles are not diagrammatically displayed from front, back, and side, as in a modern treatise, but posed as in the living body. They are given tone and movement and provided with a background such as they would have in life. This method is used with all the artist's skill. It was his own; nor need we discuss the share that any other artist, Calcar or another, had in the drafts, for the artist's mind that conceived them was that of Vesalius.

Vesalius was trebly equipped for his task: first, by a wonderful native genius for anatomical observation and classification; second, by great powers of imagination exalted by contact with high models of Renaissance art; third, by an admirable education directed along humanist lines by some of the ablest humanists of the day. But he was also most happily constituted for his task by the *lack* of certain qualities which would have handicapped him in that age. Philosophical or theological problems were far from him. He was not at all given to the drawing of those vague physical analogies typical of the men of his time, who borrowed much of this sort from Aristotle. From diversion into the miraculous or magical he was saved by a mind stocked with what he actually saw and did. Vesalius was a thorough extrovert; of stable, unsubtle, constructive, yet restless mind; with an artist's eyes, hands, and imagination: the very type and exemplar of the modern man of science. The work of Vesalius is thus great in a very different sense from that of Copernicus. The *De revolutionibus orbium celestium* is a foundation work of modern astronomy and displaced the medieval view of the Macrocosm, but it is a feat of ratiocination rather than observation. The *De humani corporis fabrica* is a foundation work of modern biology and displaced the medieval view of the Microcosm, but its vast treasury of direct observation is set forth in a systematic and orderly fashion and in the full modern manner. If one took certain parts of it, correcting a few errors, it would read like a series of articles in a modern scientific journal. Thus it is fair to claim that it is not only a foundation work of modern science but also the first modern scientific book. In this additional sense it opens the modern period of science.

TUBERCULOUS EMPYEMA

Tuberculous empyema is only too familiar to those undertaking the treatment of pulmonary tuberculosis. Any contribution to the prevention and treatment of this unfortunate complication, in terms of general principles or of technical details, is to be welcomed. We are glad, therefore, that three opening papers read at a recent meeting of the Tuberculosis Association are now in print.[1] The preventive treatment of the condition, especially as it occurs during artificial pneumothorax, was stressed by Dr. C. Hoyle. A pneumothorax is often maintained when adhesions are preventing proper collapse of the diseased areas of the lung, and the incidence of empyema is high in this type of case. Unless the restricting adhesions can be divided by cauterization, the pneumothorax should, as a rule, be abandoned. Once an empyema has developed, a primary consideration is the presence or absence of a secondary pyogenic infection. Only very rarely may a secondary infection die out or be overcome by local and general chemotherapy; but no reliance should be placed on this. The correct procedure is to secure proper surgical drainage at once and, whenever possible, to proceed to an early thoracoplasty.

While there is fairly general agreement on this, there is greater difference of opinion on what should be done for the simple forms. All the speakers were agreed that the best possible treatment is to obliterate the infected pleural space by inducing expansion of the lung by aspiration and pleural lavage, preferably with an antiseptic. Unfortunately this happy result is achieved in only a small percentage of cases. Either the lung will not expand completely or the presence of uncontrolled active disease in it makes this undesirable. If the pulmonary condition does not demand permanent collapse it is proper to give a trial of aspiration and lavage. Dr. W. C. Fowler made some useful practical observations on this. He laid down that every case should be treated from the start with the idea that a thoracoplasty may be needed sooner or later. Punctures for lavage should therefore be made well away from the possible operative field, and preferably high up in front of the chest wall above the level of the fluid. With the aid of a thoracoscopic trocar and cannula, a rubber catheter or a suction tube can be passed down to the bottom of the pleural space and masses of debris which would never pass through an ordinary needle can be sucked out. A thoracoscope may also be inserted for inspection of the cavity. A puncture made high up in this way heals safely and quickly, unlike the usual puncture made at a low level, which is expected to heal in a bath of residual tuberculous pus. The development of tuberculous sinuses, often with extensive infection and cold abscesses of the chest wall, is a grave complication of an already serious condition, and if Dr. Fowler's technique were followed many of these distressing results would be prevented.

Opinion is sharply divided between the need for radical treatment and the continuance of conservative treatment in those cases that do not respond to simple aspiration and lavage. Oleothorax has but few supporters. The late Dr. Chandler[2] made a plea for recognizing that in a small proportion of cases a purulent collection may become encysted and harmless, or even beneficial, as a sterile plomb. While this may sometimes occur, it is unsafe to rely upon it; and it is very difficult, if not impossible, to pick those cases which might be expected to follow such a benign course. Continued conservative measures, especially in the presence of disease of the underlying lung, expose the patient to the risk of the grave complications of rupture into the lung and of secondary infection. Mr. R. C. Brock quoted figures from the literature and from his own series in favour of early thoracoplasty when conservative measures have failed. Woodruff,[3] reporting on 154 cases of tuberculous empyema from Saranac Lake, had found that "of those patients who originally had a non-contaminated tuberculous empyema and who did not die of it, 30% finally developed complications either by perforation or by secondary infection." Of the 154 patients 64 were known to be dead at the time of the follow-up, a mortality of 42%. In Mr. Brock's series conservative treatment yielded very poor results, the mortality being 44%, almost the same as in Woodruff's series. In the secondarily infected group the mortality in patients not strong enough to undergo thoracoplasty was over 90%. Thoracoplasty gave very good results in simple tuberculous empyema, there being only one death in 21 patients. In the secondarily infected group the mortality of thoracoplasty was 29%; sound healing was achieved in 15 out of the 35 survivors.

It is clear that thoracoplasty combined with drainage is the only thing that holds out hope to the patient with a secondarily infected tuberculous empyema. The problem is more difficult in the uncontaminated case. The advocates of conservative measures point to their few successful cases, perhaps forgetting those which have progressed to fistula, secondary infection, and death. Those who advocate radical treatment by thoracoplasty consider the results to be so much better, and the mortality so much lower, that such treatment is clearly indicated whenever conservative treatment has failed after a fair trial.

[1] *Brit. J. Tuberc. Dis. Chest*, January, 1943.
[2] *Brit. J. Tuberc.*, 1942, **36**, 103.
[3] *J. thorac. Surg.*, 1938, **7**, 420.

PARATYPHOID FEVER

It is becoming increasingly evident that paratyphoid fever exhibits many differences from typhoid fever in its epidemiological features, as Sir William Savage[4] has shown in a study of forty outbreaks in Great Britain due to *Bact. paratyphosum* B. The incubation period is variable and, in general, shorter than it is in typhoid. As well as being a milder disease, the case mortality in paratyphoid is lower, approximating to the case mortality of *Salmonella* food-poisoning. Although characterized by an insidious onset, a proportion of attacks are initiated by acute gastro-intestinal symptoms simulating acute food-poisoning. As in typhoid, the portal of entry of the paratyphoid bacteria is through the intestinal lymphatics, and during the incubation period they multiply in the liver, spleen, and mesenteric lymph glands. A bacteriaemia initiates the onset of symptoms, and excretion of the organisms soon follows into the intestine via the bile. Contrary to the older conception, it is considered that Peyer's patches are then invaded, because it has been shown that the intestinal mucous membrane is in itself an efficient barrier against direct bacterial invasion. There is a tendency to a summer prevalence of paratyphoid outbreaks comparable with the seasonal incidence of *Salmonella* food-poisoning. Infected foodstuffs were responsible for 80% of the forty outbreaks, and half of these were traced to cream or cream cakes. Water was rarely a vehicle, and shellfish were not once implicated. Search of the literature reveals very few outbreaks of paratyphoid B fever that could be proved conclusively as water-borne. There was the Brixworth outbreak mentioned in Sir William's series, with only four cases, and Hippe

[4] *J. Hyg.*, Camb., 1942, **42**, 393.

described a small outbreak on a farm in Schleswig-Holstein. There was gross and continued pollution of the water with sewage in both instances. Paratyphoid bacteria survive in sewage and sewage effluents for a considerable time. That infection has been traced to cream is interesting, for it is probably a good medium for growth when the temperature is fairly high; but more information is required on this point. Cream is a vehicle that affords ideal opportunities for infection from a specifically infected food handler, and although cream, particularly the artificial kind, is manufactured by but a few firms, it is distributed over a wide area before it is further processed and introduced into cakes and pastries.

There is no doubt that the number of notified cases of paratyphoid fever forms only a small proportion of the total infected. There are many mild undiagnosed cases, and examination of more than one outbreak has revealed many infected persons without symptoms. The most frequent sources of infection are the ambulatory unrecognized case and the bacterially infected person without symptoms, rather than the chronic carrier, who is the usual source of infection in typhoid fever. A proportion of cases remain as temporary carriers, but we do not know the percentage of patients who become chronic—that is to say, who continue to excrete the organisms for more than a year after convalescence. Paratyphoid B bacteria have, however, been isolated from crude sewage and unchlorinated effluent at Epping for nearly ten years after the outbreak of 1931. Apart from 22 cases in 1933 traced to infection of cows' udders with sewage, no abnormal notification of cases has occurred in this locality in spite of the persistence of this reservoir of infection. When searching for the source of infection, close attention must be paid to dates and past and clinical history of the suspected carrier. The agglutination test is of considerable value, and O, H, and Vi agglutinins should be separately estimated; consistently low titres are of considerable significance. *Bact. paratyphosum* B is generally considered a human parasite, but there is evidence recently from Scandinavia that dogs may become infected. Sir William Savage explains the differences in the epidemiology of paratyphoid and typhoid fevers by considering *Bact. paratyphosum* B as a true *Salmonella* in an evolutionary stage. This organism must be present in large numbers for a successful invasion of the tissues; thus, water-borne infections are rare unless the contamination is massive, while vehicles in which the organism is able to multiply are frequent causes of outbreaks.

TOXIC PROPERTIES OF INDIUM

Indium is a silver-like ductile metal, untarnishable by air and unaffected by water, which, owing to its substitution for other less readily available metals, now finds increasing use in industry for plating by electrodeposition. Its three best-known compounds are the trichloride ($InCl_3$), the sulphate ($In_2(SO_4)_3/9H_2O$), and the sesquioxide (In_2O_3). The last is used chiefly in glass manufacture, while indium cyanide is also used as a plating solution. Therapeutically, indium has been tried in the treatment of trypanosomal and spirochaetal infections. Earlier animal experiments have established the fact that indium is indubitably toxic and have indicated the nature and site of its toxic action. The lethal dose of indium citrate by subcutaneous injection was found to range from 0.06 g. per kg. body weight for mice to 2 g. per kg. for rabbits, and by oral administration from 1.2 g. per kg. for rats to 2 g. for rabbits. Death from asphyxia was preceded by hind-leg paresis, rapid and spasmodic respiration, and convulsions. Some indication was given by these experiments that indium, like thallium, had a depilatory action. A more recent investigation[1] has attempted a closer approximation to conditions of industrial exposure to indium, and has included an examination of its possible effect as a skin irritant on both animals and human beings. The results of application of indium cyanide to the shaved skin of animals are particularly interesting, because indium cyanide represents the chief indium risk in industry. Local caustic action was followed by rapid death, but control experiments with sodium cyanide showed that this severe toxic action could not be attributed to indium, but rather to the cyanide component, as the same effect was obtained with equal amounts of sodium cyanide, and no such injury followed the application of indium chloride or sulphate or of metallic indium. Subcutaneous injection of indium sulphate and chloride in amounts varying from 2 to 6 mg. per kg. body weight caused, especially in rabbits, rapid anorexia and loss of weight, followed by nose bleeding, paresis of the hind legs, and twitching of the muscles—a picture similar to that of a mild degree of strychnine poisoning. Intravenous injection was followed by the same syndrome, but with a relative toxicity about four times that of subcutaneous injection. Post-mortem examination revealed widespread haemorrhage in the lungs, liver, kidneys, and ureters; inflammatory changes in the liver, kidneys, and heart; and atony of the gastro-intestinal tract and urinary bladder. The liver was the organ most severely affected. Albumin and indium were present in the urine. Blood counts, where these could be made, showed in general less severe damage than had previously been believed to occur, but there was a trend towards diminution of red cells and haemoglobin, haemolysis, and the appearance of nucleated red cells. In human beings no evidence of any skin-irritant property of indium resulted from the wearing on the forearm, for periods up to 30 days, of indium-treated silver plates. Incidentally, these experiments showed that indium diffused into silver has no anti-tarnishing effect. The depilatory action of indium mentioned in earlier experiments was not confirmed by the application of indium salts to the hairy coat of animals. From this investigation it appears that, while indium has undoubtedly toxic properties, its industrial application does not constitute a toxic hazard, even as a skin irritant.

HEALTH PROBLEMS IN THE NEW LONDON

London will be in the hands of the builder for many a long year after the war, and in a recent Chadwick lecture Dr. C. F. White, medical officer of health for the City, addressed himself to some of the health problems that will rise up with the post-war scaffolding. In spite of extensive destruction in certain areas, the London of the future will not differ very much in lay-out from the London as we have known it. Some sites which have been cleared, it is to be hoped, will not be built on; some thoroughfares will be widened, but the centre of London will bear much the same contours as before; and, although business and pleasure may be rather more decentralized, there will still be the enormous centripetal flow of population every morning. Dr. White foresees some decentralization of hospitals, but he is of opinion that the teaching hospitals and their medical schools must remain in central London, near the University. One would not have supposed that, with modern transport, this consideration carried its former weight, and indeed for many years one of the teaching hospitals (King's College) has been situated three miles

[1] *J. ndustr. Hyg.*, 1942, **24**, 243.

or more from Charing Cross. Dr. White spoke of the need for flat roofs as open spaces and the allocation of basements for the purposes of machinery and stores only. The sterilization of air by sprays and vapours, the control of air-borne infections in offices, and structural rat-proofing, which in his view is the only rat-repressive measure of permanent value, are all matters to be considered in the rebuilding of business London. But until the architects have got further on with their plans the medical officer of health cannot be very specific. Dr. White also touched on future London government. What kind of local authority can best manage London? It must not be so small that it cannot provide an efficient service, nor so large that the personal touch essential to successful administration is lost. Many present units of local government in London are too small; on the other hand, Dr. White thinks the county council is too large. It is true that the population of the county of London is more than sixfold that of the administrative county of Lancashire and nearly threefold that of the West Riding of Yorkshire. On the other hand, is density of population the determining factor? In area the West Riding could contain twenty Londons, and Lancashire fifteen. Moreover, the area of the London County Council, large as it is, is compact; it is a cartwheel structure. If the L.C.C. is too big as a unit of local government, how shall London be divided? To bisect it by the Thames, as it is geographically bisected, would be likely to introduce more complications than it solved. The problem which might well exercise the planners is not how London can be made smaller but whether it should not be enlarged by bringing in the boroughs and counties on its periphery.

PHYTIC ACID AND MINERAL METABOLISM

The rachitogenic property of cereals was first demonstrated by Sir Edward Mellanby by means of experiments on dogs. The agent responsible for this property was destroyed on boiling the cereals with 1% hydrochloric acid or by allowing them to germinate. Steenbock, Black, and Thomas[1] suggested that the phosphorus in the cereals was in an unavailable form, and that on treatment with hydrochloric acid or on the germination of the seed the organic phosphorus was converted into some more readily available inorganic form. Bruce and Callow[2] identified the organic form as inositol hexaphosphoric acid (phytic acid). Harrison and Mellanby,[3] working with dogs, found that the action of phytic acid was not only negative in that its phosphorus was unavailable to the animal but that it was positively detrimental in that it combined with the calcium of the cereal and of any other food eaten at the same time, forming an insoluble phytate and thereby removing the calcium from the food tract also. Indeed it was only after supplying enough calcium to combine with all the phytic acid present that additional amounts were available for calcification.

McCance and Widdowson[4] observed that healthy men and women absorbed calcium and magnesium much less readily from brown than from white bread dietaries, and showed that the effects of brown bread could be reproduced by adding sodium phytate to white bread. It was recognized, however, that the laxative action of brown bread might have exerted some influence on the absorption of calcium, and experiments were then carried out with brown bread from which the phytic acid had been removed.[5] They compared (*a*) a "brown" flour reconstituted from white flour and bran; (*b*) a flour mixture similar to the last but with the phytates hydrolysed enzymically to inorganic phosphates and inositol; (*c*) a mixture of white flour and bran from which nearly all the phytates and most of the products of hydrolysis had been removed; and (*d*) white flour. Each of 6 subjects (3 men and 3 women) were submitted to each of the above dietaries for periods of 7 days each for analytical work, with 3 days of preliminary feeding and several days of after-feeding on each diet. The orders of feeding were suitably "randomized." Calcium, magnesium, and phosphorus absorptions were studied. It was found that the laxative properties of the dietaries (*a*), (*b*), and (*c*) were approximately the same; that the calcium absorptions were worse in (*a*) than (*b*) and in (*b*) than (*c*), but almost the same in (*c*) and (*d*); that the magnesium absorptions improved progressively in passing from (*a*) to (*d*); and that the phosphorus absorptions were worse in (*a*) than (*b*) or (*c*) and a little worse in (*b*) or (*c*) than in (*d*).

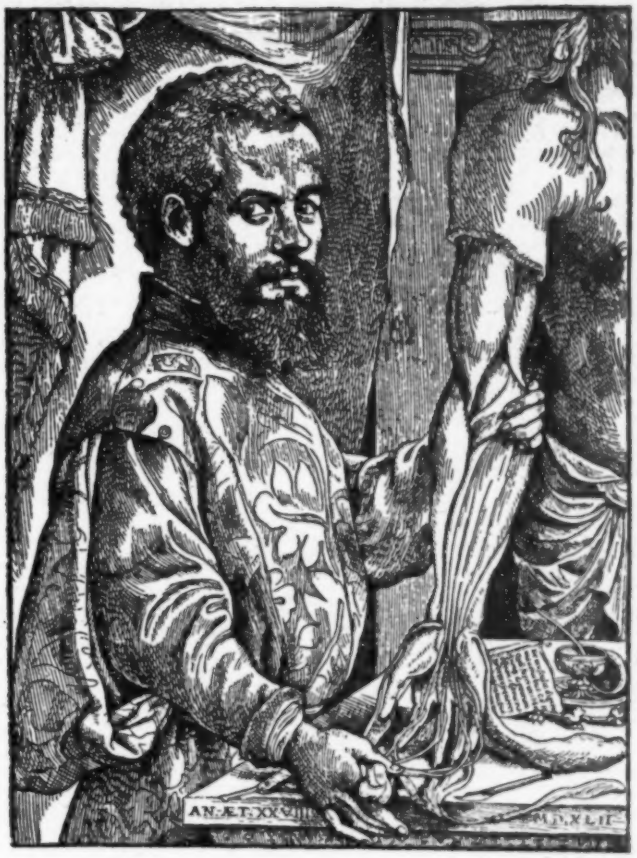
Thus Mellanby's work on puppies has been extended to human beings and the same results obtained. The addition of calcium to brown bread would counteract its only known disadvantageous property and make it unquestionably superior to white bread in all known respects.

[1] *J. biol. Chem.*, 1930, **85**, 585.
[2] *Biochem. J.*, 1934, **28**, 517.
[3] Ibid., 1939, **33**, 1660.
[4] *J. Physiol.*, 1942, **101**, 44.
[5] *J. Physiol.*, 1942, **101**, 304.

ROYAL MEDICAL BENEVOLENT FUND

For the first time for many years Sir Thomas Barlow, now in his ninety-eighth year, was absent from the annual general meeting of the Royal Medical Benevolent Fund. His place was taken by Sir Arnold Lawson, who expressed the general regret at his absence and the affection which is universally felt for him. The annual report of the Fund, presented by Dr. Lewis G. Glover, the honorary treasurer, showed a slight increase both in the subscription and the investment income. The Fund has been materially helped during the year by legacies amounting to £7,412, including a sum of £1,200 allocated by the British Medical Association as part of the bequest of the late Dr. T. C. Craig of Torquay. During the year the sum of £21,893 has been distributed in charitable assistance. The amount expended on gifts to beneficiaries, chiefly for maintenance, was just over £15,000, and on annuities £6,000. A sum of £1,277 was spent on social services and administration, and £644 on appeals and publicity. A pension scheme has been started for the staff of the Fund, with a commencing reserve of £2,000. The president, Sir Thomas Barlow, the honorary treasurer, Dr. Lewis Glover, and the honorary secretary, Mr. R. M. Handfield-Jones, were re-elected.

At the beginning of this month a number of men and women, lay and medical, Spanish, Catalan, Basque, and British, sat down to a dinner given in honour of Dr. Josep Trueta on the invitation of Señor Ramon Pereira, the President of the Casal Catala. The occasion was to celebrate the conferment on Dr. Trueta of an honorary D.Sc. of Oxford University. In response to Señor Pereira's speech of welcome, Dr. Trueta charmed his audience, in a reply mostly in English but partly in Catalan and Spanish, with a modest account of his own researches and a pleasant analogy between his technique of treating open wounds and the methods necessary to deal with political evils. In so far as there was any merit in his work, he said, tribute should be paid not to him but to Nature, whose methods of healing he tried to follow.



THE "FABRICA" OF ANDREAS VESALIUS

A QUATERCENTENARY TRIBUTE

BY

E. ASHWORTH UNDERWOOD, M.D.

Hon. Secretary, Section of the History of Medicine, Royal Society of Medicine

The month of June, 1943, marks the four-hundredth anniversary of the publication of one of the epoch-making works in all medical literature. Some time in the month of June, 1543, there appeared from the press of Joannes Oporinus, Professor of Greek at Basle, the *De Humani Corporis Fabrica* of Andreas Vesalius. It behoves us at this time to cast our minds back through the centuries, and to view in the light of later discoveries the work of this ardent reformer of anatomy and pioneer of the scientific spirit.

Vesalius was born in Brussels on Dec. 31, 1514. The son and descendant of court physicians and apothecaries, he received the thorough classical education of the age, studied medicine at Montpellier and Paris, and then settled for a time at Louvain. In these schools the trammels of the Middle Ages had not yet been broken by the spirit of the Renaissance. Anatomy was taught according to the views of Galen; and, indeed, apart from the work of Mundinus two centuries before, and by then largely forgotten, there had been practically no development in anatomical thought throughout the Middle Ages. Mundinus published in 1316 a short work—in Latin of course—called *Anathomia*. Roth, the biographer of Vesalius, considers that it is well arranged and rich in "positive" anatomy. The terminology of Mundinus was derived mainly from the old Arabian writers. As an anatomist he had the virtue of carrying out his dissections in person, but as the years passed the professors who succeeded him undertook less and less of the practical work. An Italian translation of the *Anathomia*—the *Fasciculo di Medicina*—was published in 1493, and a remarkable illustration in that book shows the method of teaching anatomy two decades before the birth of Vesalius. The duty of the professor was to comment from the altitude of his "chair" on the writings of Galen, while his assistants below him dissected the body. Students never handled the subject at all. From his childhood Vesalius had had an urge for the dissection of all sorts of animals, and with such a system of teaching he could make little headway in the study of human anatomy. Subjects for dissection were difficult to obtain, and he has left an account of one of his expeditions to steal a corpse from a gibbet. Vesalius was attracted by the new learning of Northern Italy, and in 1537 we find him at Venice, where he was in the schools with Ignatius Loyola. While he was studying there he tells us that he treated patients, "not without the greatest expectation," by the new method of the China root. When he was 23 years old he graduated in medicine at Padua, and on Dec. 6, 1537, he was appointed professor of surgery, with the direction of a school of anatomy, at that university.

The next five years were pregnant for the future of medicine. At Venice Vesalius had met a compatriot, an artist, Jan Stephan van Calcar—*insignis nostri seculi pictor*, as Vesalius calls him—and in 1538 the two men collaborated in the production of six anatomical diagrams. Such "fugitive sheets" had been not uncommon in previous years, but those of Vesalius were anatomically and artistically a marked advance on their predecessors. Although they were extensively printed and pirated, all but two bound sets seem to have disappeared. They were reprinted in facsimile—thirty copies only—by Sir William Stirling-Maxwell in 1874, and in 1920 Holl and Sudhoff reproduced them by the photostat process. Vesalius was in 1538 still largely influenced by Galen. In fact in that year he edited a revised version of the *Institutiones anatomicae* of Guinterius, a pronounced Galenist and a former teacher of Vesalius at Paris. (Five years later he will tell us in the *Fabrica* that he is able to demonstrate more than two hundred errors of Galen.) He was, however, already famous, and he had evolved the modern or Vesalian method of studying and teaching anatomy.

The 1543 edition of the *Fabrica*, apart from its superb detailed descriptions of the "fabric" of the human body, contains three features—the Portrait, the Tabulae, and the Title-page—which are of vital interest in connexion with Vesalius himself and his method. The Portrait (see Fig.) was drawn by Calcar—

as were all the other illustrations in this magnificent book. It has long been considered to be one of the finest woodcuts of its age. The head is essentially Flemish in type, and the firm thick-set lips and piercing eyes seem to throw out a challenge to the world. The dissection chosen and the text of the scroll combine to exhibit the confidence of Vesalius in his advance on Galen. The disproportions in the design have been ascribed to the conviction of Vesalius that in anatomical matters the head is more important than the hand, but Prof. Charles Singer has recently expressed the view that only the drawing of the head was by Calcar, and that the design was the work of an inferior craftsman. It is interesting to note that, of the twenty-eight oil paintings and the many other pictures of Vesalius which still exist, this *Fabrica* portrait is the only one which is considered to have been drawn from life. There is no doubt that Vesalius thought much of it; he used the original wood block

not only for the *Epitome* and the *Fabrica* of 1543 but also for the *Letter on the China Root* of 1546 and the second edition of the *Fabrica* of 1555.

The most important of the tabulae in the *Fabrica* are the three plates dealing with the skeleton and the fourteen plates of the muscles. The second muscle tabula is reproduced here. These superb drawings are really representations in line of Vesalius's conception of the science of anatomy. The body is a piece of vital mechanism, and the artist—undoubtedly inspired and instructed throughout by Vesalius himself—has positioned his dissected subjects so as to suggest the functions of the various parts. A noteworthy feature of the 1543 edition of the *Fabrica* is the landscape background in each tabula. The tabulae can be arranged in a certain order so as to give a complete panorama with a small additional picture. Reproduction gives little indication of the firmness of line and freshness of these tabulae as they appear in the original copies of the work. They certainly marked an enormous advance in the art of anatomical illustration, with the possible exception of the drawings of Leonardo da Vinci, which were not available until centuries later.

The title-page of the 1543 edition of the *Fabrica* is reproduced on page 795, but space does not permit of a discussion of the many interesting features shown by this famous woodcut. It should be noted that Vesalius is carrying out with his own hands the dissection of the female subject. The ape on the left and the dog on the right symbolize the master's readiness to use animals if the supply of human subjects failed; indeed, many of the smaller illustrations in the *Fabrica* are of animal parts, and the book contains a section devoted to experiments on animals. The erect skeleton is perhaps an expression of his devotion to osteology as the basis of the human fabric. The naked man by the column on the left—probably used for the demonstration of surface anatomy—appears clothed in the inferior drawing of the title-page to the second edition of the *Fabrica* (1555), in which other alterations were also made. This famous plate expresses to perfection the Vesalian method of teaching anatomy, and the enthusiasm with which the teaching was received by the students of Northern Italy.

With the *Fabrica* Vesalius issued an *Epitome*, which is not merely a summary of the great work. It was intended more for artists than for students of medicine, and consists of a short text followed by an anatomical atlas. The illustrations and tabulae are frequently different from those in the *Fabrica*, and they do not appear in the text itself. There is evidence that many of the *Epitome* illustrations were completed later than those of the *Fabrica*. In various places Vesalius explains that the *Epitome* is an appendix, an index, and a compendium to the *Fabrica*. The two books are twin works, each completing and explaining the other. The *Fabrica* was finished—as the dates on the portrait show—in 1542, when Vesalius was 28 years of age. It was severely criticized by some of his old teachers, and, as he tells us in his *Letter on the China Root*, in a fit of despair he burned his books and sought service with the Emperor as Court Physician. His life with the army in the wars, his ill luck over the supposed body of a corpse which came to life, and his enforced pilgrimage to Jerusalem need not detain us. He died on the island of Zante in 1564.

There is no doubt that the *Fabrica* is one of the great books of all time, although the specialized nature of its subject has prevented its wide recognition as such. In its nearly seven hundred beautifully printed pages it contains over three hundred original illustrations, many of the highest merit. The new spirit was abroad at the time, and others were working on similar lines. Eustachius of Rome had within ten years of the publication of the *Fabrica* completed a magnificent series of forty-seven anatomical tabulae, engraved on copper. A number of these were more accurate than the illustrations of Vesalius, but one has only to compare the muscle tabulae of the two men to appreciate the superiority of design and drawing in those of Vesalius. Unfortunately the tabulae of Eustachius were not published until over a century and a half after his death. To Vesalius the real advance in anatomy is due. Of numerous structures or organs—for example, the sternum, the bones of the skull, many muscles, and the uterus—he gave descriptions which were long unsurpassed. He was the first to introduce illustrations to direct attention to comparative anatomy, and in many passages he is frank enough to admit that he had not actually seen in the human the features which he describes, but had demonstrated them in apes. Anatomy, long dead, was resurrected as a science in the month of June, 1543.

On a tomb in one of the tabulae Vesalius had inscribed *Vivitur Ingenio, Caetera Mortis Erunt.* Though the remainder of his own bodily work may have perished, the spirit of his great accomplishment lives to-day. We may perhaps be reminded, not unprofitably even now, that in an age when the dead hand of medievalism lay heavy on knowledge of the human frame the whole science was born anew and advanced beyond recognition by the faith, the enthusiasm, and the unremitting labour of a single man.

I am indebted to Dr. Charles Singer and his publishers for kind permission to reproduce the three figures from his book *The Evolution of Anatomy* (Kegan Paul, Trench, Trubner and Co. Ltd., 1925).

"PORTRAIT OF A DOCTOR"

[From a Correspondent]

The B.B.C.'s series of "Professional Portraits," which has included such differing subjects as a Clydeside riveter and a district nurse, struck yet another new note in the recent portrait of "The Doctor." There is something about the medical profession which can be relied on to evoke a *frisson* from the uninitiated—the remnant perhaps of the awe of priest-craft—whether it be the thrill of wonder at esoteric knowledge or a morbid association with sickness and mortality. The best-selling value of such works as *The Citadel* must surely lie mainly in the reaction from reverence which comes from the debunking of a mystery. Stephen Potter, in his portrait of a children's physician, succeeded in presenting a real person; he certainly romanticized his subject, but contrived to do so without a touch of false glamour or a suggestion of deflation.

Certain of the portraits in this series have been built upon a basis of "actuality"—that is, by a flexible use of what might be described as the technique of the interview-cum-snapshot. "The Doctor," on the other hand, was a studio performance, played by James McKechnie (as the doctor) with a very strong supporting cast; and this choice of method was amply justified in the coherence and timing of the sequences, often no more than brief snatches of conversation, whose rapid succession built up a well-proportioned picture.

The divergent appeals of medicine as a career were brought out in the talk of a group of medical students—how to one medicine means research, to another activity among *people*, to another the following of a family tradition, and so on. The medical students were excellently cast; the crudity and immaturity of their conversation were well suggested, though necessarily in somewhat expurgated form.

In the rapid flash-back in which the doctor recalls the progressive stages of his own hospital training it may perhaps have been difficult for the layman to follow each step. Too much technical language is apt to become unintelligible, while translation into common idiom loses verisimilitude. The compromise here was effective for the most part, for while a sprinkling of technicalities remained the context was suggested in plain English.

Best among the minor studies were those of the two mothers, and it was in these sequences that one realized how, whereas most doctors have to understand and convince their patients, the children's doctor can make contact with the child only through the medium of the intervening parent. Dr. Basing justified his choice of specialization in children's diseases on the ground that here, in contrast with the treatment of adults, was to be found the study of pure disease—disease in isolation. While in adults the clinical picture is confused by social habits and the wearing out of the machine, one wonders all the same whether in children it is not equally obscured by the deceits and irrelevancies of parents, who have to be studied themselves as an important feature of the case history.

BOOKS FOR PRISONERS OF WAR

As previously announced in the *Supplement* (March 20, p. 36), the B.M.A. has sent parcels of medical books to certain prison camps where numbers of its members are known to be. It has also invited individual members who are prisoners of war to send particulars of medical books they need for private study or in connexion with their camp or hospital duties. The Association had intended to ask its members at home to contribute to a fund for supplying the books required, but in order to avoid setting up a separate war charity it has now been decided that the Medical War Relief Fund will administer money subscribed for the special purpose of providing medical books for British doctors who are prisoners of war, whether or not they are members of the B.M.A. Medical men who wish to assist this work are therefore asked to send contributions to the Honorary Treasurer of the Medical War Relief Fund at B.M.A. House, W.C.1, indicating that they wish their contributions to be devoted to the provision of books for prisoners. Only subscriptions so marked will be used for this purpose, and any unexpended balance will go to the general purposes of the Fund. It is hoped that doctors at home will respond generously to this appeal and so enable the Fund to give adequate assistance to their prisoner colleagues, particularly those who are handicapped by lack of suitable reference books in their work of treating the sick and wounded in the camps and hospitals.

SIXTH ADDENDUM TO THE "BRITISH PHARMACOPOEIA"

The General Medical Council will publish shortly a Sixth Addendum to the *British Pharmacopoeia*, 1932, in which new monographs and modifications of existing monographs will be included. Under normal conditions, when a new *Pharmacopoeia* or an Addendum to a *Pharmacopoeia* has been ready for publication, it has been customary to give facilities for advance copies to be inspected, during the three months immediately preceding publication, by medical practitioners, pharmacists, analysts, manufacturers, and others who may be interested. The Sixth Addendum to the *British Pharmacopoeia*, 1932, like the Second, Third, Fourth, and Fifth Addenda, has been prepared to deal with conditions arising from the present emergency, and it is expedient that it should be published, and thus made official, without delay.

The following new monographs will be included:

Acetomenaphthonum	Liquor Chloroxylenolis
Acidum Ricinoleicum	Menaphthonum
Alcoholia Lanae	Nicotinamidum
Chloroxylenol	Riboflavina
Dithranol	Stilboestrol
Injectio Procainae et Adrenalinae Mitis	Terpineol
Kaolinum Leve	Unguentum Alcoholium Lanae
Kaolinum Ponderosum	Unguentum Dithranolis
	Unguentum Zinci Oxidi Anhydrosum

The Addendum will contain, in addition, amendments to the *British Pharmacopoeia*, 1932, which have been made official by notices in the London, Edinburgh, Belfast, and Dublin *Gazettes*:

Syrupus Ferri Phosphatis cum Strychnina	Extractum Cascarae Sagradae Siccum
Syrupus Ferri Phosphatis cum Quinina et Strychnina	Ferri Sulphas Exsiccatus
	Paraffinum Molle Album

and emendations to the following monographs, which will become official on the date of publication of the Sixth Addendum:

Acetum Scillae	Unguentum Acidi Borici
Acidum Mandelicum	Unguentum Acidi Salicylici
Atropinae Sulphas	Unguentum Acidi Tannici
Colchici Cormus	Unguentum Aquosum
Ergota	Unguentum Hamamelidis
Ergota Praeparata	Unguentum Hydrargyri
Ferri Carbonas Saccharatus	Unguentum Hydrargyri Ammoniati
Insulinum	Unguentum Hydrargyri Oleati
Ipecacuanha	Unguentum Hydrargyri Subchloridi
Ipecacuanha Pulverata	Unguentum Sulphuris
Magnesii Trisilicas	Unguentum Zinci Oleatis
Mepacrinae Hydrochloridum	Unguentum Zinci Oxidi
Mepacrinae Methanesulphonas	
Pamaquinum	
Sulphanilamidum	

The Addendum will contain also new or revised appendices relevant to the monographs named above and an index. It must be understood that no additional monograph, or emendation of a monograph, is official until the Sixth Addendum has been published.

Reports of Societies

VASOMOTOR DISORDERS IN WARTIME

At a meeting of the Section of Neurology of the Royal Society of Medicine on May 20, Dr. R. M. STEWART presiding, a discussion was held on vasomotor disorders and immersion injuries as experienced in warfare.

Classification

Prof. J. R. LEARMONTH said that vasomotor disturbances encountered during total war assumed special importance in the surgery of the extremities; at the worst their occurrence might prejudice the survival of a whole limb, and at the least might lead to loss of digits or to loss of function. He suggested the following classification as a basis for discussion:

I. Vasomotor disorders resulting from injury. A. Arterial spasm: (1) local, after subcutaneous injury, (2) of collateral vessels (*a*) after arterial contusions with thrombosis, (*b*) after division of an artery; B. Traumatic arteritis; C. Traumatic venous thrombosis; D. After division of peripheral nerves.

II. Vasomotor disorders occurring in organic vascular disease. A. Syphilitic endarteritis; B. Arteriosclerosis; C. Thromboangiitis obliterans (1) of rapid development, (2) of slow development, (3) of stabilized type; D. Paradoxical spasm.

III. Vasomotor disorders from local effects of cold. A. Symmetrical syphilitic digital gangrene; B. Vasomotor symptoms and

signs started or accentuated by (1) change of occupation, (2) change of climate, (3) high altitudes; C. Immersion foot; D. Frostbite.

He proceeded to give some brief descriptions of cases in which vasomotor symptoms and signs started or were accentuated by change of occupation or of climate or by high altitude.

An airman aged 19 went up without gloves. At 12,000 ft. he began to suffer a "fierce ache" in hands and wrists. A few hours after landing he was quite better. After this episode he had similar attacks when above 12,000 ft., although always suitably clothed. In the third of these, and in subsequent attacks, the medial three fingers of both hands became blanched up to the proximal interphalangeal joints. Four years later, although he had been employed on ground duty only, he was still having similar attacks, which were worst in cold weather, particularly in early morning. The vasomotor responses in the digits showed digital arterioles to be in a state of spasm. Full reflex vasodilatation was not reached until the feet and legs had been heated at 45° C. for 50 minutes (normal 15 to 30 minutes), although the ultimate skin temperatures (32° to 35° C.) were high enough to exclude any notable organic narrowing of the vessels.

A patient aged 25, by occupation a cinema operator and accustomed to work in a hot environment, went to Army duty in the north of Scotland. In summer, while working on the metal of a high pylon, he had his first attack, in which all the fingers of both hands became first dead white and cold, then blue, then fiery red. During the following winter these attacks became more frequent and interfered with his military duties. On clinical examination no evidence of cardiovascular disease was found, the fingers reaching full vasodilatation level in the normal time.

On the subject of "immersion foot" Prof. Learmonth emphasized the scrupulous avoidance of a too rapid return of blood flow to the chilled parts, whether induced by local heating (e.g., during first aid) or by interruption of sympathetic vasoconstrictor fibres. He had found it useful to nurse these patients on the face, with feet and legs uncovered and elevated, by an open window in default of a fan. The surgeon's attitude must be almost rigidly conservative, and this might require much patience. Formal high amputations should be reserved for the rare cases in which gangrene had been extensive or which were aggravated by sepsis. Some form of arch support should be provided in cases of paralysis of the small muscles of the feet; this should be worn during graduated walking exercise until these muscles recovered power.

Experimental Findings in Immersion Foot

Dr. W. BLACKWOOD gave an account of some histological and experimental findings in immersion foot. The human material consisted of one foot from a man who died half an hour before rescue and of tissues from feet and legs removed from survivors from 2 to 26 months after rescue. In the majority of the later cases peripheral sepsis was present. The histological appearances suggested that at the time of immersion damage was done to all the structures in the limb of a degree and to a level dependent upon the length and severity of the exposure. In particular, damage was done to nerves and muscle, with some damage to veins. Changes in skin and bone awaited further study. The nerves had the greater proportion of their axis cylinders and myelin sheaths killed. Muscles were probably damaged directly. Haemorrhage from and thrombosis of veins and venules might arise. All these changes were curiously patchy, but increased peripherally. After rescue the nerves began to regenerate. Axis cylinders grew down slowly and myelinization took place very slowly. Organization and recanalization of thrombus occurred in the veins. Muscle might await re-innervation or be replaced by fibrous tissue.

The experimental work carried out in conjunction with Dr. Russell consisted of exposing the tails of rats to cold artificial sea water for varying lengths of time and studying the changes after rescue. Patchy damage was found to be produced in nerve and muscle. In rats recovering up to two months the nerves showed persisting partial Wallerian degeneration. The muscles showed acute patchy changes similar to Zenker's necrosis, followed by inflammatory and regenerative processes and later by atrophy due to denervation. The implication was that early changes in the human might well be similar to those seen in the rats, but early human histological material had not so far been available.

Immersion Injuries due to Cold

Surg. Cmdr. C. C. UNGLEY confined his remarks to immersion injuries due to cold. True immersion foot and immersion hand, or peripheral vasoneuropathy after chilling, followed prolonged exposure to degrees of cold insufficient to cause frostbite. There was damage to peripheral nerves, vessels, muscles, and skin. During exposure the extremities swelled and there was loss of feeling. Peripheral arteries might be pulseless for some hours after rescue, and remain so in cases going on to gangrene. This short pre-hyperaemic stage was followed by a stage of hyperaemia in which the affected parts became hot, red, painful, and more swollen, the more severe cases showing blisters and gangrene. The result of damage to nerves was evident in sensory loss, and motor, vasomotor, and submotor paralysis. In the post-hyperaemic stage inflammation subsided and vascular tone recovered, skin temperature fell, and vessels might become hypersensitive to cold. Complete recovery, which in severe cases must await complete regeneration of peripheral nerves, was often preceded by signs suggesting partial re-innervation of end-organs and effector organs. Late sequels included recurrence of pain, tingling, swelling or blisters, persistence of the cold sensitive state or of hyperhidrosis, and occasionally circulatory effects suggestive of vascular occlusion.

In describing some studies in vasomotor disorders, he said that the instability of the hyperaemia in the later weeks of the hyperaemic stage was specially noteworthy. Once the feet had become cold—as, for example, by immersion in cold water or by walking on cold stone floors—they remained cold for hours in spite of all attempts to induce reflex vasodilatation. On the other hand, if they were hot to begin with, it was impossible to induce vasoconstriction reflexly. One of the characteristics of post-ganglionic sympathectomy was that the denervated vessels became sensitized to minute amounts of adrenaline such as circulated in response to insulin hypoglycaemia. Similar sensitization was seen in the hyperaemic stage of immersion foot. As the hyperaemia was passing off, often about 6 to 14 weeks after rescue, there might develop a cold sensitive state manifested either by Raynaud's phenomenon or by coldness of the feet, which took hours to warm after return to a warm environment.

Dr. J. B. GAYLOR described a case of persistently cold limbs following shipwreck two years ago, together with lack of sensation in the foot, almost to the ankle. It was possible that the low temperature of the limbs had inhibited nerve regeneration, or that owing to impairment of blood supply there was not sufficient oxygen to encourage regeneration, even though there might be sufficient to prevent loss of tissue.

Dr. RAYMOND GREENE discussed the justifiability of interference with the nerve supply in such a condition as frost-bite or immersion foot, and whether, if interference was justifiable, it should be immediate or carried out at a later time. He gave reasons for supposing the effect of any immediate interference to be either negligible or harmful, the condition of a limb after immersion or exposure being equivalent itself to that of a limb subjected to a natural post-ganglionic sympathectomy.

Sir THOMAS LEWIS said that the observations brought forward to the Section were the first reasonable ones on immersion foot, largely because such observations could be made only in time of war. It was obvious that cold had a damaging effect on tissue. In a general way that had long been known; it was merely a question of degree of cold and the duration of exposure. He took it that a person would eventually die from exposure to cold provided the cold was sufficiently extreme and the period sufficiently long. It was not strange, therefore, that changes were found when limbs were immersed for periods of hours, or perhaps days, and that those changes should affect all the tissues—skin, muscle, nerve. It seemed clear that the vasomotor system was not exceptional in this respect, and that at a relatively early stage of recovery there were vasodilatation in response to heat and vasoconstriction in response to cold. As to whether sympathectomy should be employed, it seemed to him that sympathectomy, if it was to be attempted at all, should be carried out during the later allergic stage, which seemed to produce in some way a spasmodic condition of many of the vessels in the limbs. For some of the recorded phenomena there was as yet no physiological explanation. But facts must come first, and the physiological explanation must be sought later.

At the annual meeting of the Medical Society of London Prof. G. Grey Turner was elected president.

HYPERTENSION AND RENAL DISEASE

At a meeting of the Section of Urology of the Royal Society of Medicine on May 27, Mr. H. L. ATTWATER presiding, a discussion took place on the relation of hypertension to renal disease.

Mr. KENNETH HERITAGE said that arterial hypertension, the cause of 23% of deaths in persons over 50, was outstripping cancer as a principal cause of death. Surgical interest in hypertension, excluding associated endocrine diseases, applied in three groups of cases: (1) hypertension associated with bilateral renal disease, chiefly bilateral urinary obstruction, with or without infection; (2) hypertension associated with unilateral renal disease; (3) essential or malignant hypertension in which evidence of a primary renal lesion was absent or doubtful. Hypertension was found associated with chronic urinary obstruction due to prostatic enlargement, urethral stricture, bilateral ureteric calculi, ureteric obstruction due to inflammatory or neoplastic infiltration, and a variety of other lesions. In many, particularly older, patients this might be a chance association, but a fall in blood pressure followed by a permanently lowered level was observed often enough to be a commonplace. Although these patients were frequently of advanced age and had long-standing urinary back-pressure, the hypertension was of a particularly benign type and responded well to drainage.

Clinicians had been on the look-out for cases of hypertension with evidence of unilateral disease, in the hope of affording relief by nephrectomy. Although a dramatic fall in blood pressure often followed nephrectomy, in most cases a subsequent steady upward creep of the pressure was noted until sometimes the original reading was reached again. The unilateral lesions most often associated with hypertension were trophic pyelonephritis, hydro- and pyo-nephrosis, and vascular lesions of the kidney; but he emphasized that it was exceptional to find a gross surgical lesion associated with hypertension, and it was always possible for the association to be an accidental one. The great majority of the cases were in the third of his groups, the "unknown" or essential group, and there was no evidence that the kidney was primarily responsible for this condition.

An Unknown Factor

Dr. R. W. SCARFF said that the curious feature of the hypertension resulting from kidney damage was the inconstancy of its occurrence. Various explanations for the apparently fortuitous happening had been put forward—anoxaemia, excretory failure, or the formation of substances which directly or indirectly neutralized the action of the pressor substance. There was no parallelism between the event of hypertension and the amount of renal disability. He concluded from a survey of recent work that both humoral and nervous mechanisms might play a part in the production of hypertension, but that knowledge of these alone was insufficient to explain the inconstancy of the occurrence and the variations in the behaviour of this condition. A vital link in the chain had still to be sought.

Dr. HORACE EVANS said that there was no adequate treatment, either medical or surgical, for essential or primary hypertension. Two main groups of patients with hypertension were now recognized. In one group the hypertension was secondary to some obvious pathological state such as chronic nephritis, and in the other it appeared as the primary feature without obvious renal or other disease. Benign hypertension was a disease of later life (50–60), and ran a course of many years, often symptom-free until some cardiac or cerebral catastrophe occurred. Malignant hypertension appeared to be a separate clinical entity. It was relatively rare and found in a younger age group (40–50), with severe symptoms such as headache, dyspnoea, and visual disturbances at the onset, and in the later stages renal failure was common, with death within 12 to 18 months of onset. Papilloedema was the early physical sign which immediately distinguished this condition from benign hypertension. A careful search for unilateral kidney disease should always be made, especially in young patients. The results of nephrectomy in such patients might be miraculous, though the outcome must depend upon the presence or absence of secondary vascular changes in the sound kidney. Apart from this small group, the main group was essential or primary hypertension. Here it was of the first importance to make an accurate diagnosis of the several disorders which had so much in common in their later stages. He referred to the "hotch-potch" of conditions which masqueraded under the designation of chronic interstitial nephritis, including late stages of Bright's disease, malignant hypertension, chronic pyelonephritis, and late-stage pregnancy kidney. Particularly important was the separation of benign and malignant hypertension. A period of careful observation of symptoms, blood-pressure readings, optic fundi, and renal function was essential. Until an effective therapy was introduced it was probably true to say that the majority of patients with hypertension were better without treatment unless the state of the heart demanded it.

Errors in Search for "Surgical Kidney"

Mr. DICKSON WRIGHT spoke in particular of some errors which had followed upon the enthusiastic search for the surgical kidney in hypertensive subjects. These on occasion might be serious, even endangering the life of the patient. (1) Pyelography had been over-interpreted and minor variations and kinks had been given an exaggerated importance. (2) Kidneys might be extirpated on the basis of minor pathology to cure hypertension, with no result, so that the patient lost a good kidney and was left to fight a largely renal disease with only one kidney—a sad state of affairs. Nephrectomy was not indicated unless the kidney concerned had practically no function left or nephrectomy was indicated *per se*; in each case the operation of splanchnic and lumbar sympathectomy and possibly adrenalectomy should be done there and then, because if the patient fell among the 70% who were unaffected by nephrectomy one had at any rate done something else for his hypertension, and he required only one operation more to complete the treatment on the other side. (3) The kidney exposed at the first splanchnic resection might be found to be grossly diseased, and although pyelography might be normal the surgeon might be tempted to remove it there and then, to refrain from splanchnic resection on account of the gross renal pathology, or to go back and remove the diseased kidney later if sympathetic surgery failed. Mr. Wright described cases illustrating these points. One of them illustrating the first and third of these alternatives was the following:

A woman aged 26 had severe eclampsia with her third child and was left with malignant hypertension. Course downhill in spite of all treatment. At her first sympathectomy kidney found to be markedly granular, with a raspberry-like surface. Agreed with physician that first kidney would come out later if bilateral sympathectomy a failure. At second sympathectomy the other kidney looked normal, but a biopsy was done, and the section was indistinguishable from that of the grossly diseased kidney; both showed gross renal pathology. If biopsy had not been done a serious error might have been made.

The importance of the surgical kidney should be written down rather than up. A biopsy of the renal parenchyma in hypertension should always be made. The sympathetic nerves in a renal operation should always be cut if hypertension was present.

In a Chadwick lecture on "Plants causing Irritation," with Sir WILLIAM J. COLLINS, M.D., in the chair, Mr. F. J. CHITTENDEN said that a considerable number of plants met with wild, or cultivated in gardens in England, were apt to irritate the skin or the nose and eyes of those handling them. Some, like *Primula obconica*, were well known to be suspect, but many were unsuspected, and sometimes the result of contact with them was not only irritation but general discomfort and, for the time being, incapacity for work. These symptoms had not infrequently been attributed to other causes, with failure to obtain relief. The study of such afflictions was complicated by the well-ascertained fact that, while some persons were susceptible to irritation by one plant, others suffered far less from it or might escape altogether, though susceptible to irritation from some other plant. Most of these disorders, except for the various forms of hay-fever, only followed actual contact with the foliage or stems of the irritating plant, and some of the primary causes of irritation acted only through wounds in the skin. The wounds might be very minute, like those made by the hairs of the stinging nettle, or, in very thin skins, by the needle-like crystals abounding in the sap of the daffodil and many other bulbous plants. Knowledge of the range of plants capable of causing such troubles might give pointers in the search for the causes of some obscure skin affections, or of running at the eyes and nose, and a chance of avoiding them.

Correspondence

Psychotherapy in General Hospitals

SIR,—Dr. Dalton Sands's article and your editorial of May 22 have raised vital issues. Dr. Rees and Dr. Shepley express disapproval of the policy advocated, while Dr. Dillon warmly supports it. I venture to suggest that the issue, as raised by these correspondents, is a false one. Indeed it would seem as if we were witnessing the unedifying spectacle of competition within the profession for the privilege of treating a certain group of patients.

Putting aside such subsidiary questions as the feelings of relatives and the so-called "stigma" of the mental hospital, we have to deal with a single fact in reality—namely, the inevitable locked gate of the mental hospital and all that it rightly represents in the way of legal supervision and protection. The locked gate is for certain patients necessary, for others unnecessary; for some it is helpful, for others the reverse. The therapeutic resources on both sides of the locked gate should be equivalent. They are far from being so now, and in consequence we have the anomalous situation of patients being persuaded to pass the locked gate by the assurance that though they have no need of supervision or restraint yet only behind the locked gate can the necessary treatment be secured. Conversely, if, as some of us hope, therapeutic resources, such as electric convulsant therapy, become generally available at open hospitals, we shall have to face increasingly the pleas of patients, relatives, and often family physicians: "If the proper treatment is available at the general hospital, surely the patient needn't be condemned...."

It follows therefore that psychiatrists will be called on to make more definite diagnoses of what may be roughly defined as certifiability, and on that issue *alone* to decide the disposal of the patient, in the full knowledge that the decision will not limit or even modify therapeutic possibilities. And it may be hoped that, if such a state of affairs is achieved, the psychiatrists on both sides of the locked gate will co-operate with good will and an objective outlook on clinical realities.—I am, etc.,

London, W.1. H. CRICHTON-MILLER.

SIR,—Dr. T. P. Rees and Dr. W. H. Shepley in their letter (June 12, p. 735) make several statements which are open to criticism.

First I should like to point out that, having been a member of the medical staff of a mental hospital for many years, I am well aware of the extremely good work which goes on in such hospitals, and I should be the first to deprecate the fact that mental hospitals should be used solely as dumping grounds for the chronic, incurable patient. On the other hand, I maintain that there are many types of patient who are definitely unsuitable and unwilling to enter mental hospitals on a voluntary basis because of the impossibility of complete segregation. Many of those suffering from neuroses and early psychoses (socially well conducted) resent going into mental hospitals, as even though they are housed in separate villas or admission units in the mental hospital they of necessity meet the chronic patients on common ground—viz., at occupation, recreation, in the grounds, etc. Would Dr. Rees and Dr. Shepley prefer that these patients, therefore, because of their unwillingness to enter a mental hospital, remain untreated until they become certifiable, or their illness becomes so chronic that the chances of recovery are considerably diminished and in any case is probably prolonged by months?

Secondly, this hospital makes no claim for the originality of the methods of treatment employed. Dr. Rees and Dr. Shepley state that these methods were already proved in the modern mental hospital. This is rather a sweeping statement. Are they proved? I, personally, am not convinced that such methods of treatment as electro-convulsive therapy, insulin, etc., are not still in the experimental stage, and that many more years of research are necessary to *prove* these methods. Did they originate in Warlingham or other mental hospitals? So far as I know, they were first employed in American and Continental neuropsychiatric clinics and were then tried out in this country.

The fact that the number of admissions to Warlingham Park Hospital has increased from 125 in 1932 to 277 in 1942 is somewhat surprising, as throughout the country the number of admissions to mental hospitals has decreased appreciably during the war years. Why, then, does the Croydon area differ in this respect?

Regarding the financial aspect, I agree with Dr. Sands that many of these cases, if treated later because of their unwillingness to enter a mental hospital in the early stages of their illness, would have required prolonged hospitalization involving more economic distress to their dependants and a heavier financial burden to be borne by the hospital. The comparison of the maintenance rate at Sutton with that of a mental hospital established in peacetime and built as such is hardly fair. This hospital was an upgraded institution which had to be adapted for hospital purposes and is continually being adapted at the present time. In my opinion, after this war there will be a place in psychiatry for the neuropsychiatric clinic in the general hospital, psychiatric units for acute and short-term disturbed cases, and for the mental hospital. The last would still have a cross-section of all psychiatric cases and continue to carry on the good work which it is doing at the present time.—I am, etc.,

Emergency Hospital, Sutton. LOUIS MINSKI.

Selecting the Medical Student

SIR,—So it seems that the planners are now getting busy with the prospective medical student. No longer will boys or girls say that they are going to be doctors, but must wait until they have been before a board to see if these mandarins will allow them to be so. Suppose a candidate is rejected, is there to be any appeal? Will he be told why he is not suitable? Then suppose the rejected tries something else, is another board going to tell him he can't be that?

Let us get rid of these attacks on our freedom before it is too late, and we find we are a nation of spineless individuals with no say in our future or that of the children. It is an astonishing fact that such interference should be suggested, and is a sign of the times, when all initiative and liberty are being taken from the public. Personally I should not presume to tell anyone what his future career cannot be. With much more interference the press gang is more likely to be needed to gain entrants to the ranks of the medical profession.—I am, etc.,

Sheffield. J. A. WOOD.

Planning of Medical Education

SIR,—Dr. C. F. V. Smout, in his letter (May 29, p. 676), offers destructive criticisms of a few of the suggestions put forward in my article on medical education (May 1, p. 547). These criticisms, apart from indicating an attitude of complacency and satisfaction on the part of Dr. Smout, are largely invalid, in that their author has indulged in the practice of lifting a statement from its context and ascribing to it a significance not intended in its proper setting: this applies in particular to his remarks on co-ordination of the anatomy of the body as a whole. I hoped that I had made it clear that the time saved by rendering unnecessary the repeated revision of minute details would be available for such correlation; at present the student is fully engaged in acquiring new minute details and attempting to revise ones already noted right up to the eve of his professional examination, and it is common experience that he has no time to take a broad view of the human body and acquire a thorough understanding of the important principles involved. Then Dr. Smout asks, "Who *is* placing a premium on feats of memory?" May I *truthfully* reply that both Dr. Smout and myself are sinners in this respect?

Dr. Smout accuses me of being out of date regarding the relationship between universities and the Ministry of Labour. I can assure him that no school is more strict than my own in its duty to the State in this connexion, and would inform him that his horizon must be limited if he is unaware of the large number of students in Great Britain who descended from degree to diploma in the immediate pre-war days; although war

measures have temporarily diminished this number, this does not affect the ultimate issue.

Finally, with regard to Dr. Smout's complaint concerning the length of time required to interview prospective entrants, I would impress on him that the importance of this interview of a person on the threshold of his proposed life's career is becoming generally appreciated, and, while a proportion of the candidates may be eliminated by means of the entrance examination, coupled with a survey of their previous records (as envisaged in my communication), even if the time devoted to interviewing the remainder approaches that calculated by Dr. Smout, it would be time which, in the view of many, would be extremely well spent. In effect, I hope Dr. Smout will turn his mind towards constructive effort, as I am sure he must be aware of the widespread dissatisfaction felt concerning the present state of affairs.—I am, etc.,

University of Sheffield. F. DAVIES.

Future of Medical Services

SIR,—Our medical Peers and Dr. Charles Hill by their statesmanlike and practical speeches, reported in the *Journal* of June 12, have so qualified the discussion on medical services that we must all feel grateful to them. We seem to have been delivered from a state of hopeless confusion that had little apparent prospect of decision; there has been of late a tendency to widen again the closing gap between preventive and curative medicine, but these speeches should help to stop such a disastrous move.

What private practitioners, consultant or general, are anxious to know is: What form will local authority take, and in what way, if at all, will it interfere with their professional lives? It appears that these influential speakers envisage a local authority, not our present-day county or municipal council, but an *ad hoc* health authority which may well be so constituted as to be democratic and acceptable to the medical profession. It has often been stated that there is no urgent need to set going any new scheme, and the Dawson Consultative Council more than twenty years ago was of opinion that the only satisfactory way of finding out what was wanted and what could be done was to set up an experimental health centre.—I am, etc.,

Westbury, Wilts. CHAS. E. S. FLEMMING.

Doctors and the Future

SIR,—Mr. A. B. Rooke and his co-signatories (May 22, p. 649) asked the very question to which I have tried, without success, for some time to obtain an answer. I beg your indulgence and valuable space, since no one has yet answered this group their vital and very pertinent question, to ask this question again: Since the Government considers a drastic reorganization of the medical profession and extensive changes in the conditions of medical practice urgently necessary, can we not be told what it is considered that is wrong now?

It might seem to many of us that this explanation is a prime necessity, owed to us at the outset, and one that should have been made clear at the beginning before the discussion of schemes started. It is not doubted that there is room for great improvement, nor can it be questioned that great improvements have steadily evolved since the last war, but there will still be room for further and continuous improvement even after any new Government scheme for a comprehensive medical service has been brought in.

A second question arising out of the above is: Who is really behind this desire for drastic change? Is it purely political? I know of no such agitation or demand on the part of the general public.

Lastly, since the present National Health Insurance scheme is, at the moment, the chief form of State medical service or scheme, why is not this scheme to be modified, and, building on the existing foundations, made a really first-class, comprehensive, and complete medical service for the bulk of the populace? In the present panel scheme we have at least the nucleus of what could be made a comprehensive medical service for the great majority. Is the N.H.I. scheme to be "washed out"? As Lords Dawson and Horder have so wisely urged, we should build upon existing foundations, and gradually improve and evolve. It is not a happy augury for the Government's future scheme that their existing one (N.H.I.) should be a byword in many respects; for it is still rather regarded as an insult than an honour to be termed "panel"! Millions of our people are ashamed of belonging to it.—I am, etc.,

Hassocks. CHARLES A. H. FRANKLYN, M.D.

Proposals and Discussions

SIR,—The Secretary of the B.M.A. and the Chairman of Council have ruled that to question whether the country or the profession wants the Beveridge plan is to challenge the British Constitution, since Parliament—*vox populi*—has tentatively accepted the proposals. This is a specious argument bearing no analysis. It is all a question of what is reasonable. Parliament has no more right to coerce the medical profession against its will than it would have to order Anglican clergy to practise Roman Catholicism. Trade unionism is a direct consequence of the recognition of the right of the worker to a hearing.

At the joint meeting held on March 31 last the Chairman of Council said: "The Council regarded the Beveridge report as of such importance as to call for reports on its proposals from certain of the standing committees." Would it be impertinent to suggest that the proposals are of such importance as to justify an inquiry of the whole profession? Such an inquiry is expected as of right of membership of the B.M.A. There is, in more senses than one, no doubt of the way in which the Ministerial mind is working. The present position is that whatever Bill is presented to Parliament will possibly meet with the approval of half a dozen members of the discussions committee. But there is no more guarantee that the Bill would be modified in deference to popular medical opinion than that the original proposals for a State Medical Service will not be introduced.

On Feb. 13 last it was announced that special meetings were to be held on March 31. The motion to be debated, as framed, afforded a very poor occasion for full discussion, but it gave some the opportunity to contradict Sir William Beveridge. However (perhaps by skilful tactics), the Minister precipitated Council into entering into "discussions," thus effectively depriving the rank and file of the profession of their only chance of an expression of opinion. The Beveridge report is a major political issue, and, while it is clear that the Minister intends to introduce legislation at the earliest moment practicable, it is equally clear that he will not risk a Governmental defeat. Thus his primary concern is the possible reaction of about 400 Members of Parliament, while the reactions of about 40,000 practitioners are as much "in the discard" as the preliminary discussions. Had this not been so the Minister would have continued to attend all the discussions in person.

The demand for a Royal Commission had a salutary effect, for the committee was able to negotiate the postponement of the White Paper. This was reported in the *Daily Telegraph* as a "concession to doctors." It was nothing of the sort. The question of a State Medical Service had not arisen. The withdrawal of the request for a Royal Commission was, however, a concession to the Minister in consideration for his undertaking to honour his promises. Meanwhile we must wait impatiently to learn the basis of the continuing discussions. I will hazard the guess that the basis is the Draft Interim Report of the Medical Planning Commission, about which the Chairman of Council said at the last Annual Representative Meeting "there need be no fear that anything would be done without full consultation."

Much has been said of unity in the profession. Unity cannot be achieved without acknowledgment of other points of view. Unity is the basis of stolid government the very foundation of which is based upon the existence of an official opposition. This is the sort of thing the British Constitution provides for. It should not be beyond the ability of Council to devise some similar machinery. Applied to Representative Meetings, the effect would be stimulating to thought and conduct. Unity is achieved by sinking differences after they have been acknowledged to exist. Council must by now be strangely lacking in this respect. Had the profession been consulted earnestly and promptly the Minister would never have dared to trifle with us. Had propaganda been wisely directed, the doctors would not yet be judged as seeking concessions. At this eleventh hour the effort to achieve unity would still be small,

but the purpose remains very high. As matters stand the Minister will make proposals calculated to meet with the approval of Parliament. That will be that.—I am, etc.,

Watton-at-Stone. MAURICE E. WIGFIELD.

"In the Discard"

SIR,—I would like to draw attention to the most timely warning you give in the last sentence of your excellent leading article under this heading (May 29, p. 670) and also to endorse your advice to read the report of Dr. Charles Hill's speech (*Supplement*, May 22).

The Beveridge Assumptions C and A and the housing question will most certainly exercise the minds of those who have to find a living to a much greater extent than will problems of health or education. Unemployment and bad housing will never allow of "positive health"; to offer the electorate a nationalized medical service instead of work and proper shelter would be grossly unjust and intolerable. It is unnecessary to repeat here all the reasons against a whole-time salaried service; but as a vote of almost 90% was cast against such a service at the A.R.M. in 1942 it behoves those of us who are of this mind to continue to support, actively, those of our officials and leaders who have shown that they appreciate that this is not the best way in which we can render our services to the community.

However well it may work in some special services, the State official (or local government authority official) can be no substitute for the "family doctor." Of this the patients are well aware from past experience. Our new "publicity" must warn the people that, in spite of the promises of politicians, the imposition of such substitution has been the basis of Ministerial proposals; whereas B.M.A. proposals are based on the best interests of the individual patient.—I am, etc.,

Chester. DAVID R. OWEN.

Radiologists and the Future

SIR,—There are some points in Dr. Norman Henderson's letter (June 5, p. 710) that call for comment. The replies to Dr. Henderson's questionary indicate that 57% of the radiologists prefer to continue their private practice in their own rooms, while the replies to the questionary issued by the Faculty of Radiologists show a majority of 2 to 1 in favour of conducting their diagnostic *x*-ray private practice in their hospital or hospitals. This disparity is possibly explained by a difference in the type of practitioner consulted. The membership of the Faculty is restricted to those exclusively engaged in radiology in one or more of its branches, and the Faculty's questionary was submitted to its members only. Dr. Henderson's questionary was submitted to a wider field, including medical men engaged in general practice as well as radiology. In reply to the Faculty's questionary an overwhelming majority of radiotherapists expressed their agreement with concentration of all radiotherapy, private and hospital, into large units. Regional organization as outlined in the Memorandum on Planning of Radiotherapy for Great Britain issued by the Faculty is in keeping with that opinion and with present-day needs.

The Faculty is one of the appointing bodies to the Medical Planning Commission organized by the B.M.A., and subscribed to the general principles embodied in the Interim Report of that Commission, in which respect it is in agreement with the great body of medical opinion in this country. The Faculty, in its Memoranda on Radiodiagnostic and Radiotherapy Services for Great Britain, certainly supports the principles of regional organization of those services, but there is nothing in either memorandum to warrant Dr. Henderson's suggestion that it favours the idea of a whole-time salaried State Medical Service.

The mainspring of Dr. Henderson's recent activities seems to be an apprehension that the interests of radiologists are not being watched in these times of impending change, but as he is not a member of the Faculty he is perhaps not fully informed of how much the Faculty has been doing in this respect. Its members have been consulted by questionary on the broad principles involved; its Council has been in arduous session throughout the past three years, has submitted the two Memoranda above mentioned, and has, at the request of the Goodenough Committee on Medical Schools, produced two further reports on radiological education. The Faculty is in close co-operation with those bodies charged with negotiation with the Minister on the medical service of the future, and at the invitation of the Joint Committee of the three Royal Colleges has appointed a committee, which is now in session, to advise on radiological matters.—I am, etc.,

S. COCHRANE SHANKS.

London, W.1. President, Faculty of Radiologists.

Haemolysis in Blackwater Fever

SIR,—I have just received your issue of March 6 and read the paper on haemolysis in blackwater fever by Felix Smith and R. Winston Evans (p. 279) with very great interest. In these days of disruption it is obviously not easy to get at files of the smaller journals, and so I attach no blame whatsoever to the authors for believing that their alkaline treatment is a "new rationale for the treatment of intravascular haemolysis." I enclose a reprint of my paper on "The Biochemical Aspect of Blackwater Fever" from the *West African Medical Journal* of as long ago as July, 1932. This reprint gives the alkali treatment in great detail, and I still insist on the importance of glucose in the matter. Up to 1934 I knew of thirty-four cases treated as I advocate and there was one death. Since then I have treated four cases in Jamaica with no deaths.

In the same mail *Nature* of Feb. 27 contains a letter from Maegraith, Findlay, and Martin, who are in West Africa, in which the authors announce their discovery of a red cell lytic enzyme in organs which include the liver and spleen, and an enzyme which occurs in serum and tissues. Such a discovery follows the rule of enzyme action, and the sites of production are exactly those that would be postulated by the reasoning in my paper of 1932.—I am, etc.,

Kingston, Jamaica. W E. MCCULLOCH.

Tuberculosis and Exposure to Infection

SIR,—Your correspondent Dr. Basil Sampson (June 5, p. 708) happens to have forgotten the factor of personal resistance in his remarks on bovine tuberculosis in South Africa, which illustrate the common tendency to assume that everyone exposed to tuberculous infection will sooner or later become tuberculous. Although it may be good policy to regard everyone so exposed as potentially tuberculous, it is common knowledge that only a small fraction of such persons develop tuberculosis. Whether they do so or not depends partly on inheritance, but largely on habits and conditions of life; and where there is evidence of exposure to such infection, these constitute the first thing to investigate and if necessary to set right.

In spite of the great advances made in diagnostic technique, there is still need for a good laboratory test to distinguish between those who are beginning to develop tuberculosis and those who are in no such danger.—I am, etc.,

Farnham, Surrey. F. R. WALTERS.

Advice on Sterility

SIR,—It is difficult to understand why Dr. R. H. P. Hick is so annoyed with Lord Horder. On his own admission he sends his sterile patients to a gynaecologist, who investigates the couple more or less completely and sends them back to Dr. Hick with reports and advice as to treatment. This is precisely what the medical officer at a clinic does if the patient is sent there by a general practitioner. But what of all the unhappy couples who are not so blessed as Dr. Hick's patients and whose medical advisers shrug their shoulders and say, "Go home and keep on trying," or, to the wife, "You could have a D and C done"? With regard to this business of numbers—though numbers are necessarily used at clinics, as in hospitals, for purposes of filing and records—it may ease Dr. Hick's mind to know that the patients themselves are invariably addressed by their proper name and title. Are clinic doctors necessarily more inhuman and unsympathetic than gynaecologists, and is the sweeping statement that "a State Medical Service is unwanted by doctors and patients" true? It is nice to know of the faith that Dr. Hick's patients, no doubt justly, repose in him, and of how successfully he and his gynaecologist collaborate to fight sterility, but it may be pointed out that if a couple is by them ranked as sterile "after even a few months" this may account for a proportion of their successes. Incidentally, how

is our knowledge about this exceedingly complex problem to grow unless there is some co-ordination of methods and accurate recording of observations over a period of many years?—I am, etc.,

Crediton, Devon. MARGARET C. N. JACKSON.

Oedema of Extremities at Sea

SIR,—In the matter of Dr. H. E. Thorn's letter (June 5, p. 708) on oedema of the feet and ankles in fit men during a voyage, may I offer the conjectural fruit of my experience? I was on a liner for four years which crossed the Tropics every month, and this oedema was a regularly recurrent trouble in hot weather. So far as the crew were concerned—and they were supposed to be fit men—it often affected the same members voyage after voyage; it was confined to the victualling department—i.e., stewards, cooks, etc.—the deck and engine-room departments did not suffer. Rubber soles were an obvious factor in every case; habitual "scurriers"—e.g., bedroom and saloon stewards—were the worst victims; leather soles or cold weather relieved the condition. All the passenger accommodation on this ship—cabins, alley-ways, and public rooms—was decked with some rubber compound, and from these and other facts I came to the conclusion that the main cause was the insulation which this and the rubber soles made complete, and that an accessory one was the friction on the sole and dorsum of the foot which the abrupt rubber to rubber contact on walking created. So far as troops on transports are concerned bare feet for at any rate part of the day are the best preventive and cure.—I am, etc.,

Beckley, Sussex. C. G. LEAROYD.

Nasal Intubation

SIR,—I have never been able to understand the objection by the rhinologists to this method. Is it because it was developed by the anaesthetist and not by the rhinologist? The article by Mr. A. R. Dingley (June 5, p. 693) is interesting, but it gives no more than the usual precautions which every anaesthetist takes when he employs this very useful procedure. Mr. Dingley admits very few complications, and at the same time suggests "lack of anatomical knowledge of the nasal cavity," faulty technique, etc. If an anaesthetist does not possess the anatomical knowledge—which I very much doubt—or is guilty of faulty technique, it is no reason why the method should be condemned. I think there is very little danger of doing harm if reasonable care is used—and it should be used in all procedures. I have seen much more damage done by the inexperienced during the oral approach than I have by the nasal one. I have seen one or two sanguinary encounters when an inexperienced anaesthetist has spent his time removing divots from the pharyngeal wall. Nasal intubation by a Magill tube is, to my mind, quite safe with reasonable care, and I have seen a life saved by the method when a lung abscess ruptured into a bronchus. The anaesthetist had not time to assemble the laryngoscope, but intubated blindly and suctioned. The patient made an uninterrupted recovery.

Mr. Dingley cites two cases which are of special interest: the first where the enthusiastic anaesthetist produced two pints of blood from the nose, and a second where a case of adenoids was nasally intubated. These two cases were obviously instances of wrong technique, but they did nothing to condemn the method. I think the method is ideal for oral surgery and especially for difficult dentistry.—I am, etc.,

J. B. H. HOLROYD,
Anaesthetist, Sheffield Royal Infirmary.

SIR,—Mr. A. R. Dingley in his article on nasal intubation (June 5, p. 693) says: "It is clearly unwise to pass a tube through a nasal passage the interior of which is a closed book to the introducer." I would point out that the experienced anaesthetist, when passing a nasal tube, gently explores the nasal airway, and can diagnose by means of his tube the nature and position of any obstruction that he may meet without inflicting injury on the mucous membrane, in the same way that a surgeon may diagnose the type and position of an obstruction in the urethra by means of a sound or catheter. This renders unnecessary the previous visual examination of the nasal airway, which Mr. Dingley advises should be done after cocainization and with a head lamp.

Mr. Dingley gives no figures, but hints that virulent sinus infection is not very uncommon after nasal intubation for tonsillectomy. In my experience it is not common or virulent, one mild sinus infection having occurred in 500 cases (all soldiers) which were nasally intubated for tonsillectomy. Hewer in *Recent Advances in Anaesthesia* quotes 500 consecutive cases of nasal intubation for tonsillectomy without a complication sufficient to prolong the patient's stay in hospital.—I am, etc.,

Colchester. DOUGLAS CLENDON.

Social Insurance and Medical Practice and Research

SIR,—Dr. E. M. Fraenkel, in his most interesting and suggestive letter (May 8, p. 583), points to the important part which university clinics on the Continent have played in scientific research. May I add that the part which sickness insurance on the Continent has played in this matter is just as notable. While, under the British system of health insurance, approved societies and insurance committees were hardly in a position to show much interest in the progress of scientific research and its socialization, the municipal and other sickness funds on the Continent have regarded this part of their duties as the most essential one.

Let me quote for this a description which Dr. G. F. McCleary, formerly a deputy senior medical officer of the Ministry of Health, has given in his book on *National Health Insurance*, 1932, page 53: "The General Local Sickness Society in Hamburg, for instance, has four institutes for artificial sunlight therapy, where about 7,000 persons are treated annually, and a large orthopaedic institute to which is attached a workshop for making appliances. Diagnostic facilities are provided on a large scale. The Institute of the Association of the Berlin Krankenkassen (sickness funds) contains chemical, pathological, bacteriological, and serological departments, and makes 5,000 to 6,000 examinations monthly. The miners' benefit societies have founded a number of hospitals, many of which are models of their kind, for the special needs of the population." No wonder, then, that, as McCleary observes, "the extensive range of the medical services provided by the German scheme brings the insurance societies into close relation with the great body of the medical profession in Germany."

To all those who, in common with the views often expressed by the International Labour Office in publications on social insurance, emphasize the organic, and indeed dynamic, link between medical science and sickness insurance administration, it must come as a shock that the Beveridge report aims at widening the gap already existing in this country between social insurance and medical practice and research. Social insurance funds will be entirely "separated" from medical service and research, to which they will only contribute just as a tax-payer contributes to the needs of the country. The ambition of local sickness funds to set up—in their own interests as well as in the interests of a higher human aim—the best possible service and to attract to it the best men of practice and research will be eclipsed in favour of a State scheme, of which we cannot say when it will come, what its comprehensiveness will be, and how far it will leave open the door for individual exertion so necessary in that great science—medicine.—I am, etc.,

Richmond. HERMANN LEVY.

V.D. in the Merchant Navy

SIR,—I welcome Dr. J. C. H. Browne's exposure (May 22, p. 645), after a first-hand experience of it as ship surgeon, of the discreditable state of affairs that may still obtain at some ports and times to impede the proper medical care of the merchant seaman infected with venereal disease. Now Dr. Browne records his observations of the dire results to seamen, and the public health, of the absence of hospital accommodation for venereal disease at ports, and the interruption of other peacetime arrangements for continued treatment at ports of V.D. in seamen; while the third year of war found us in full and public agitation over the increase of V.D., especially in seamen and in the populace of our ports.

I feel sure that medical opinion can rightly be unanimous in pressing for: (1) in all ports, facilities for treatment that do in fact facilitate the seaman's finding treatment and keeping under it; (2) instruction in V.D. of the medical profession in

general, and the ship surgeon in particular; (3) proper equipment for adequate treatment of V.D. in ships that carry surgeons; (4) serious consideration to be given to the fact that in ships that carry a surgeon only a minority of seamen who have cause do consult him for suspected or apparent V.D., although the seaman heartily dislikes visually apparent V.D. either in himself or in his shipmates.

Since the very great majority of ships carry no surgeon the seaman, by long-established custom, keeps his ailments for medical attention when he gets ashore—if by then they still distress him. The idea of treatment on board ship is perhaps still foreign to the merchant sea-going profession. Moreover, in the past, treatment of V.D. on board ship could be, at best, only inadequate; it was hardly better on shore; and while the last three decades have brought a great improvement of treatment, it has lagged at sea far behind the standard on shore. There is still some foundation for the traditional idea in the seaman's mind that not much benefit will accrue to him from bothering the ship surgeon on such a matter. The main barrier, however, keeping him from the ship surgeon in the matter of V.D. is dislike and suspicion of its being logged against him—as by law it must be if his ship surgeon deals with it. The same seaman, however, evinces no objection to the hospital doctor's logging V.D. against him in a clinic's records, even when done in his presence. The ruling difference appears to be not only that the clinic is publicly pledged to secrecy—though that is highly valued—but also that the hospital doctor is not his boss, and the clinic books are not open to inspection by bosses—master, mate, owner—as is the ship's log. Easy to understand, not easy to reform, yet reformed it ought to be.—I am, etc.,

H. M. HANSCHELL,
Director, V.D. Clinic,
Albert Dock Seamen's Hospital.

London, E.16.

The Contaminated Injection

SIR,—Your annotation on the contaminated injection (May 15, p. 608) draws attention to the problem of filling a hypodermic syringe with sterile air under adverse surrounding conditions, and suggests a cumbersome procedure as a solution. The problem is simply overcome by using a platino-iridium needle and a spirit lamp. A platino-iridium needle can be raised to a white heat in a spirit flame without harm, and while holding its point in the flame and at the same time withdrawing the piston you have a medium through which sterilized air can be drawn and which no spore can withstand. I have used this method many hundreds of times without harming the needle or the glass syringe. It has the added advantage that the same needle can be used where many injections have to be given at one sitting, it being perfectly sterilized each time. The ordinary needle could be used in the same way in an emergency, but it would be quickly ruined by such treatment.—I am, etc.,

M. J. SAUNDERS.

Portland.

Universities and Colleges

UNIVERSITY OF MANCHESTER

A one-day course of lectures on health in the factory has been arranged for industrial managers on Sunday, July 4, by the Extra-mural Department of the University in conjunction with the Association of Industrial Medical Officers. The course begins at 10.45 a.m., when Dr. H. Trumper will speak on the responsibility of management for the health of the worker, followed at 12 noon by Dr. T. M. Ling on psychological factors in industrial health. At 2.15 p.m. Mr. G. P. Barnett will speak on management's part in accident prevention.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

The following candidates have passed the Primary Fellowship Examination:

R. C. Bell, D. T. A. Brown, B. N. Catchpole, B. S. Crawford, J. F. Dark, F. X. Darne, J. R. G. Edwards, E. J. Field, J. P. Haile, A. G. Leacock, R. I. T. Lloyd, S. T. McCollum, R. A. C. Owen, V. G. Patel, R. D. Richards, Mary F. Richardson, R. B. K. Rickford, F. Robinson, K. E. D. Shuttleworth, G. F. Smart, J. B. L. Taylor, G. T. Watts, M. R. Williams.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

Sir Henry Dale, G.B.E., P.R.S., will deliver the Frederick Price Lecture on "A Prospect in Therapeutics" in the Hall of the College on Friday, July 2, at 5 p.m.

Obituary

SIR ARTHUR NEWSHOLME

Dr. J. D. ROLLESTON writes:

The sympathetic obituary of this great man in the issue of the *Journal* for May 29 has an important omission—namely, the lack of any mention of his keen interest in the alcohol problem. For many years he was a member of the Society for the Study of Inebriety and Drug Addiction, and in 1927-9 was its president. In 1928 he attended the 19th International Congress against Alcoholism held at Antwerp, where he delivered a masterly address on "The Place of the Alcohol Question in Social Hygiene." His *International Studies* (1931) contain an instructive account of anti-alcohol activities in Denmark, Sweden, Switzerland, Italy, Yugoslavia, Poland, and Czechoslovakia, while his work on *Red Medicine* (1933) gives a description of the campaign against alcoholism in Soviet Russia.

Sir FRANCIS FREMANTLE, M.D., M.P., writes:

Your tribute to Sir Arthur Newsholme mentions his work on tuberculosis. I would remind your readers of his report to the Local Government Board and his article in the *Journal of Hygiene* (July, 1906, **6**, No. 3) showing the special influence of segregation in workhouses and workhouse infirmaries in the reduction of the phthisis death rate. The breadth of his inquiry in this and other countries, the thoroughness and honesty of his statistical evidence, the credit given to other known factors, the searching criticism of accepted argument, gave a new and convincing proof of the value of the abused Poor Law and of institutional treatment as such. As a young county M.O.H., on a pilgrimage to him at Hove some 40 years ago, I had much valuable advice, of which one phrase has endured: "Study vital statistics, Fremantle; they will prove anything you want." I always wondered if he meant "prove" in the Pauline sense.

The following appreciation of EDWARD HARTE, M.B., B.Ch., D.P.H., deputy medical officer of health, Harrogate, comes from Dr. D. Derry Payne, medical officer of health, Harrogate, and Dr. J. Tudor Lewis, medical officer of health, Barnsley: We would not wish the recent sad death of Dr. Edward Harte to pass without paying a tribute to his strong character and great personality, qualities which enabled him to bear the bludgeonings of a hard fate with a laugh and a joke. We first knew him when he joined the public health staff in Croydon. A slowly progressive illness "accidentally discovered" had caused him to give up his practice in Blackpool. After taking his D.P.H. he entered the Public Health Service and very soon became a great success. When one of us went to Harrogate as M.O.H., Harte soon followed as deputy. He was outstandingly successful with children, and the mothers all had an abounding confidence in him. To the many administrative problems of a public health department he brought a sane common sense, and he had the gift of making himself liked by all his colleagues, medical and lay. What attracted people most was perhaps his great spirit and sense of humour. He could and did see fun in everything, and his quickness of phrase and richness of expression were astonishing. Although he knew he was doomed we never once heard him complain of his fate; he rather liked to joke about it, and when he got a retinal haemorrhage he was amused and laughed that his senior colleague "had bought a pup." This was typical of Harte. Reading was his main relaxation, but at one period he had played a good game of golf. He was also a very keen bird-watcher, and his knowledge of this subject was extensive. We have lost a dear friend and a valued colleague. The profession generally and the Public Health Service in particular will be much the poorer by his untimely passing.

Dr. W. HENDERSON STEPHEN died at Southend-on-Sea on May 28 in his 75th year after a long illness. A graduate of Aberdeen in 1891, and of farming ancestry, he had fought his way by his own tireless industry and settled, first at Preston, and later, for 20 years, at Smethwick, where he built an outstanding practice by his thoroughness and by his kindness, cheerfulness, and sense of humour. He had been an ardent Territorial, serving 1914–16, and retiring as lieut.-colonel. Settling in partial retirement at Southend, he again achieved a successful practice until two years ago, when his health failed. He had been a member of the B.M.A. for nearly 50 years and was a past chairman of the South Essex Division.

Medical Notes in Parliament

THE GOVERNMENT'S PROPOSALS

Dr. RUSSELL THOMAS on June 10 drew attention to the negotiations between the Minister of Health and the medical profession. He said the House should have some idea of these before the White Paper was published. At a meeting on May 16 the Deputy Secretary of the B.M.A., Dr. Hill, spoke on the proposals put forward by the Minister. Put briefly, these were that medical men would cease to practise freely as doctors and would become whole-time employees of local authorities. If this happened doctors would form a service of technicians controlled by men and women ignorant of medical matters. The objections to the local authority arrangement had been set out by Dr. Anderson, Secretary of the B.M.A., in a letter to the *Times*. The main objection was that the medical profession would be in the hands of the local authorities, people who were frequently under the influence of party politics, and could not understand the vital personal relationship which existed between doctor and patient. In any case the scheme put forward by the Minister would lack the comprehensiveness which was an essential of the Beveridge plan. The proposals for a consultant service were vague. They were to be centred in a hospital. The appointment would be by the local authority and would be full- or part-time. The Minister said there would be compensation for practices, but no details were given. The money invested in practices was between £50,000,000 and £100,000,000. This was dismissed in the Minister's proposals with small consideration. The *British Medical Journal* had said it almost looked as if the Government wished to claim absolute control of the general practitioner for strict supervision of certification by the doctor. The upshot of it all was that the medical profession turned down further discussion of the proposals as completely unfruitful. They demanded a Royal Commission, but after further consultation that was set aside. The negotiations up to date had done incalculable harm through the whole rank and file of the medical profession.

Dr. MORGAN said Dr. Russell Thomas's speech was the essence of medical stupidity. The present negotiations were non-committal and exploratory. The Minister depended too much on the B.M.A. and leant toward bureaucracy. The present medical system was no credit to this country. It was completely uncoordinated. He wanted the Minister to negotiate with other bodies, medical as well as lay; to have in mind the principle of no public finance without lay control; and that medical education should be brought within the purview of some authoritative body.

Discarded "for the Present"

Mr. ERNEST BROWN said they dealt with a gigantic national issue—a question of the whole administrative structure of a comprehensive health and hospital service. It included the relation between the municipal hospitals and the voluntary hospitals. In February the Government had announced its acceptance of Sir William Beveridge's Assumption B. That meant that it announced its decision to go ahead with the preparation of a comprehensive medical service for the whole country. There was need for speed, although there was no need for haste. Several major issues demanded decisions soon. The country would want to know what was to be done with the Emergency Medical and Hospital Service when the war came to an end. The Government also had a duty to the large body of medical men and especially young medical men now in the Forces and to their future. Whatever conclusions they came to they would need good will. They were now in the preliminary stage, in which he sounded representatives of the medical profession, the major local authorities, and the voluntary hospitals to find out how their minds ran on the various issues, and to put before them ideas of his own. They had not reached the main discussion stage, which would be followed by legislative proposals when the Government had come to its conclusions. The second stage he still desired to be one of full and open review of the subject both in Parliament and elsewhere among the organizations, professions, and persons likely to be affected, including many now serving in the Forces. For this stage discussion might be more fruitful if he put before the House an appreciation of the main issues which gave everyone something to bite on.

Dr. HADEN GUEST: Without commitment?

Mr. BROWN: Certainly, at that stage. That would be the stage at which they could find out the feelings of the general public, who were to be the patients of this service. The third stage was the introduction of draft legislation, when the Government would have to make up its mind what was the right and practicable measure to introduce to Parliament. Since February he had arranged with representatives of the medical profession and the voluntary hospitals to embark on the preliminary and informal exchange of ideas. The medical representatives consisted of a group of medical men and women brought together by the B.M.A. and the Royal Colleges. This Representative Committee agreed with him to discuss and exchange ideas in confidence and without commitment. The committee was not his appointment, but that of the profession. He had put a number of ideas to it, including some on a possible salaried basis for general practice in a comprehensive service. He invited the committee's own criticisms and counter-suggestions. After a number of meetings the committee suggested that the whole subject should be referred to a Royal Commission. They discussed the suggestion but agreed that the previous exchange of ideas should be resumed. Disproportionate attention had been directed to certain phrases such as that about the "discard." The committee had understood him to mean that if it would advance discussion he would discard for the present any ideas so far considered and would consider each further issue quite afresh. The discussions had been resumed. He was sure they would continue to be helpful. Fairly soon he hoped to publish a statement, perhaps as a White Paper, to afford a focus for all concerned. They ought not to take final decisions until the man-in-the-street and the individual doctor in practice or in the Forces had a full chance to consider the main issues fairly. He was amused to see it suggested that the Government intended to dragoon one of the oldest of the learned professions into a corps of "State lackeys," or to deny the ordinary individual the elementary right to have his say in choosing his medical adviser.

The House then adjourned for the Whitsuntide Recess.

Enemy Attacks on Hospital Ships

In the House of Commons recently Mr. A. V. Alexander, the First Lord of the Admiralty, circulated a list of hospital ships which had been sunk or damaged by the enemy, as follows:

1940:
- May: *Atlantis*, off Norway, bombed four times, no damage.
- " *Brighton*, Dieppe Harbour, bombed three times, sunk.
- " *Maid of Kent*, Dieppe Harbour, bombed, destroyed by fire.
- " *St. Andrew*, nr. Calais, shelled twice, no damage; nr. Dunkirk, bombed twice, no damage.
- " *St. Julien*, Dunkirk; off Calais and in Downs, shelled twice, bombed once, no damage; on passage to Dunkirk, bombed and machine-gunned, slight damage.
- " *St. David*, off Gravelines, shelled from shore batteries, no damage; off Dunkirk, bombed, shelled, machine-gunned, no damage.
- " *Worthing*, off Calais, shelled twice, bombed once, no damage.
- " *Isle of Guernsey*, off Calais, shelled from shore batteries, no damage; on passage to Dunkirk, bombed and machine-gunned, slight damage.
- " *Isle of Thanet*, off Calais, shelled from shore batteries, damaged; English Channel, bombed and machine-gunned, no damage.
- " *Dinard*, off Dunkirk, shelled once, bombed once, slight damage.
- June: *Worthing*, nr. Dunkirk, bombed and machine-gunned twice, severe damage.
- " *Paris*, on passage to Dunkirk, bombed three times, sunk.

1941:
- Jan. and Feb.: *Dorsetshire*, off Sollum, bombed once, machine-gunned once, no damage.
- " *Aba*, Tobruk Harbour, bombed, slight damage.
- April: *Aba*, Suda Bay, Crete (at anchor), bombed, slight damage.
- May: *Aba*, Canea, Crete, machine-gunned, slight damage; on passage to Haifa, bombed twice, damaged.
- April: *Vita*, Tobruk, bombed twice, damaged; on tow in Mediterrancan, bombed, badly damaged.
- " *Ramb IV*, nr. Tobruk, bombed, slight damage.
- Aug.: *Amra*, Gulf of Suez, torpedoed from aircraft, no damage.
- Sept.: *Karapara*, Tobruk, bombed, damaged.
- " *Dorsetshire*, Port Tewfik, bombed, slight damage.
- Nov.: *Llandovery Castle*, Suez (in dock), bombed, slight damage.
- Dec.: *Somersetshire*, between Tobruk and Alexandria, dive-bombed and machine-gunned, no damage.

1942:
- Jan.: *Somersetshire*, between Tobruk and Alexandria, dive-bombed, no damage.
- Feb.: *Somersetshire*, Tobruk Harbour, bombed, no damage.
- " *Llandovery Castle*, between Alexandria and Tobruk, bombed three times, no damage.
- Mar.: *Llandovery Castle*, Tobruk Harbour, bombed, slight damage.
- April: *Somersetshire*, between Alexandria and Tobruk, torpedoed, severe damage.
- May: *Ramb IV*, nr. Alexandria, bombed, sunk.

To this list must be added the *Centaur*, torpedoed and sunk a few weeks ago by the Japanese, with a loss of 268, including ten nurses, in addition to the matron, and, according to some reports, eighteen medical officers.

All these ships were properly marked in accordance with the Geneva Convention.

Investigations into Incidence of Tuberculosis

Mr. DOUGLAS on May 27 asked the Minister of Health whether any national survey had been undertaken to ascertain the effects of poor housing conditions and of malnutrition upon the incidence of tuberculosis. The MINISTER replied that reports were published before the war by the National Association for the Prevention of Tuberculosis on "Causal Factors in Tubercu-

losis" and "Tuberculosis and Social Conditions in England," and the association was at present conducting an inquiry into the relation between malnutrition and tuberculosis. The subject was also mentioned in the M.R.C. report issued in October last on "Tuberculosis in Wartime." Various lines of medical research were being officially pursued on the general question of nutrition, which might prove to throw some light on the particular question of the incidence of tuberculosis.

National Health Service Proposals

Mr. HOGG on June 3 asked whether the Minister of Health, in view of the misapprehensions resulting from his negotiations with the B.M.A. on his proposals for a National Health Service, would renew the Government's assurance that Assumption B of Sir William Beveridge's report still formed part of the Government's policy. Mr. BROWN: Yes, sir.

Medical Examination at Detention Barracks.—Sir JAMES GRIGG, answering questions on May 18 about detention barracks, said regulations on the medical examination of soldiers sent to detention barracks were clear and explicit. A military court of inquiry would examine whether they were generally observed at Chatham detention barracks. The medical officer of this barracks had been transferred elsewhere.

Increase in Short-term Sickness.—Mr. BROWN said on June 3 that there had been an increase in the incidence of short-term sickness among the insured population. He had no evidence to suggest that the increase was attributable to long hours of labour and to fatigue resulting from Civil Defence and Home Guard duties.

Notes in Brief

According to the latest figures in the Ministry of Health there are some 4,100 maternity beds in voluntary institutions, 8,000 in municipal homes and hospitals, and over 3,000 in the emergency maternity homes established by the Department, making a total of between 15,000 and 16,000 beds in England and Wales.

Of members of the Forces discharged owing to disability and whose claims for pensions have been rejected about 17% have been cases of psychoneurosis.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* during the week notifications of whooping-cough, diphtheria, and scarlet fever fell by 89, 82, and 76 respectively, but those of measles rose by 273.

Diphtheria was less prevalent throughout the country, a drop of 31 in Staffordshire being noteworthy. Scarlet fever was down by 32 in Yorks West Riding, 31 in Lancashire, and 31 in Staffordshire. Whooping-cough pursued a less steady course than diphtheria or scarlet fever, notifications being 71 fewer in Lancashire, 36 in Staffordshire, 29 in Warwickshire, and 28 in Middlesex; the largest rise was in London, 36.

Within the counties the largest increases for measles were in Monmouthshire 122, Oxfordshire 105, Essex 95, Lincolnshire 93, Northamptonshire 78, Somersetshire 71, and Glamorganshire 53. The biggest falls were in Norfolk 100 and London 64. This was the eighth consecutive week for which a decline has been recorded in London; the notifications have dropped from 1,166 to 365 during the period.

Additional cases in existing outbreaks accounted for a rise of 9 in the incidence of dysentery. In Warwickshire, Birmingham C.B., the cases rose from 3 to 23; in Gloucestershire, Bristol C.B., from 8 to 12; and in Cornwall, Bodmin M.B., from 3 to 9.

In *Scotland* scarlet fever notifications fell by 48, those for cerebrospinal fever rose by 10, the returns for Glasgow mounting from 5 to 14. An outbreak of dysentery has been reported from Edinburgh involving almost 100 cases, the majority being pupils and teachers at a school and residents in a university hostel.

Quarterly Returns for Northern Ireland

During the first quarter of 1943 the birth rate was 24.3 per 1,000, compared with an average of 19.7 for the five preceding first quarters. Infant mortality was 85 per 1,000 registered births and was 14 below the five-years average. The general death rate was 15.0 per 1,000 and was 1.1 below the rate for the March quarter of 1942 and 2.6 below the average rate for the first quarters of 1938-42. Deaths from pulmonary tuberculosis numbered 254 and other forms 86; the five-years average was 270 and 72. 231 deaths were attributed to the principal epidemic diseases, compared with 437 for the average of the preceding five first quarters.

The Week Ending June 12

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,966, whooping-cough 2,063, diphtheria 607, measles 6,724, acute pneumonia 637, cerebrospinal fever 50, dysentery 127, paratyphoid 6, typhoid 5.

No. 22

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended June 5.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1943 (a)	(b)	(c)	(d)	(e)	1942 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	79	7	31	5	6	127	9	38	2	3
Deaths		2	—				—	2		
Diphtheria	630	37	160	66	31	583	23	179	39	25
Deaths	9	3	7	—	—	8	1	2	—	2
Dysentery	125	8	35	—	2	100	8	45	—	—
Deaths			—	—	—			—	—	—
Encephalitis lethargica, acute	6	—	—	—	—	1	—	1	—	—
Deaths		—	—				—	—		
Erysipelas			47	9	—			46	7	2
Deaths		—	—					—		
Infective enteritis or diarrhoea under 2 years				33					44	
Deaths	51	13	4	13	6	32	1	10	4	1
Measles	7,668	365	517	23	44	7,279	856	1,003	109	373
Deaths	1	—	1	—	1	12	2	3	1	1
Ophthalmia neonatorum	107	10	30	1	1	111	3	28	2	1
Deaths										
Paratyphoid fever	6		2			10	—	1	1	
Deaths	—	—	—		—			—		—
Pneumonia, influenzal*	768	42	5	2	15	794	43	3	—	5
Deaths (from influenza)	6	—	2	—	—	15	2	2	—	—
Pneumonia, primary			213	20				236	23	
Deaths		19		6	8		29		6	10
Polio-encephalitis, acute	2	—				1	—			
Deaths		—					—			
Poliomyelitis, acute	5	—	1		—	1	—	1		—
Deaths		—	—				—	—		
Puerperal fever		3	9				2	18		
Deaths		—			—		—			—
Puerperal pyrexia†	169	16	26	2	2	170	10	20	4	2
Deaths		—		—					—	
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,921	168	220	54	54	1,058	41	217	74	13
Deaths	—	—	1	—	—	—	—	—	1	—
Small-pox	—	—	—		—	—	—	1		—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhoid fever	4		1	10	1	5	1	4	10	1
Deaths‡	—	—	—	—	—	1	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	1	—
Deaths			—	—	—			—	—	—
Whooping-cough	2,144	151	226	17	46	1,137	103	65	29	11
Deaths	11	—	3	—	1	8	1	1	—	—
Deaths (0–1 year)	310	48	67	38	23	331	36	68	21	25
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	3,949	556	573	199	127	4,263	551	596	197	114
Annual death rate (per 1,000 persons living)			12·9	13·1				13·4	13·2	§
Live births	6,501	762	1041	431	321	5,868	639	890	382	282
Annual rate per 1,000 persons living			21·3	28·3				18·4	25 5	§
Stillbirths	228	22	23			224	17	44		
Rate per 1,000 total births (including stillborn)			22					47		

* Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

† Includes puerperal fever for England and Wales and Eire.

‡ Includes paratyphoid fever for England and Wales and London (administrative county).

§ Owing to evacuation schemes and other movements of population, birth and death rates for Northern Ireland are no longer available.

The Services

Brigadier R. M. Luton, M.C., Canadian Army, was appointed C.B.E. (Military Division) in the Birthday Medical Honours.

Fl. Lieuts. G. D. Graham and N. Livingstone, R.A.F.V.R., have been appointed M.B.E. (Military Division).

Capt. J. W. Logan, R.A.M.C., has been awarded the D.S.O., and Capts. J. D. Dow, E. J. Kerr, and Lieut. R. G. Boyd, R.A.M.C., have been awarded the M.C. in recognition of gallant and distinguished services in North Africa.

The following medical officers have been mentioned in dispatches: Group Capt. C. T. O'Neill, O.B.E., and Wing Cmdr. L. Freeman, R.A.F.; Squad. Ldrs. W. A. S. Falla, A. Wilson, R. G. D. Forward, R. G. Griffiths, W. Hopkins-Jones, Fl. Lieuts. O. T. Brown, N. G. Farrell, and A. Russell, R.A.F.V.R.

The *London Gazette* announces the appointment to O.B.E. (Civil Division) of Capt. (temp. Major) WILLIAM BRUCE KIRKLAND, M.B., B.S., Chief Medical Officer, Northern Territory Medical Service, Commonwealth of Australia. The announcement reads as follows: During the air raids on Darwin Dr. Kirkland was in charge of the hospital and was continuously on duty. In very difficult circumstances and with only broken equipment he remained for some weeks to deal with the air-raid casualties. After the first air raid many patients were successfully evacuated to safer accommodation. Dr Kirkland rendered outstanding services in conditions of grave danger.

CASUALTIES IN THE MEDICAL SERVICES

Prisoner of War.—Capt. H. A. Deverell, R.A.M.C.
Died.—Lieut.-Col. H. R. Pomroy, A.A.M.C.
Officially Reported Prisoner of War.—Surg. Lieut. A. P. Curtin, R.N.V.R.
Killed.—Surg. Lieut. J. H. Graves, R.N.V.R.
Reported Missing in North Africa.—Capt. I. E. W. Gilmour, R.A.M.C.
Prisoner of War in Japanese Hands.—Lieut.-Col. T. Hamilton, A.A.M.C.

Medical News

A joint meeting of the Nutrition Society and the Food Group (Society of Chemical Industry) will be held on Saturday, July 3, beginning at 11 a.m., at the London School of Hygiene and Tropical Medicine, when the subject of discussion will be "Milk." The chair will be taken by Prof. H. D. Kay, and papers will be read by Mr. J. L. Davies ("The Production, Supply, and Marketing of Milk"), Dr. A. T. R. Mattick ("Bacteriological Aspects of Milk Processing and Distribution"), and Dr. S. K. Kon ("The Chemical Composition and Nutritive Value of Milk and Milk Products"). The participants in the discussion will include Dr. W. R. Wooldridge, Prof. A. W. Ashby, and Prof. G. S. Wilson.

Under the auspices of the Association of Austrian Doctors in Great Britain Dr. A. Czech will give a lecture on "The Past and Future of Austrian Health Services," with lantern slides, on Thursday, July 1, at 6 p.m., in the Conway Hall, Red Lion Square, W.C.1. Guests will be welcomed.

Surgeon Rear-Admiral Cecil P. G. Wakeley will present a talking cinematograph film, illustrating first aid in the Navy, in the Council Chamber, the County Hall, West Street, Chichester, on Saturday, July 3, at 3 p.m.

The Derry Gardens, on the top of the well-known store of that name next to Kensington High Street Station, will be open on behalf of St. Bartholomew's Hospital from July 5 to 10 inclusive.

The trustees of the Lady Tata Memorial Fund announce that, on the recommendation of the Scientific Advisory Committee, they have agreed, if circumstances permit, to make the following awards for research in blood diseases, with special reference to leukaemia, in the academic year beginning on Oct. 1, 1943: grants for research expenses—Dr. J. Furth (New York), Dr. P. A. Gorer (London), Dr. A. H. T. Robb-Smith (Oxford), Prof. L. Doljanski (Jerusalem); part-time personal grant and grants for assistance and research expenses—Dr. W. Jacobson (Cambridge).

Official information has been received that Drs. W. Ainslie, R. E. Anderson, M. C. Bain, H. Allan, R. I. Macbeth, J. M. Sclater, and C. S. Wilson have been interned in Changi Camp, Singapore.

In the *Journal* of June 5 (p. 701) we printed an appeal for funds for a British Hospital to be built in Stalingrad. Since then medical men have sent in a number of donations, which now amount to £400. No donation is too small, and we hope that doctors will not hesitate to dip their hands into their pockets for an object so worthwhile.

Letters, Notes, and Answers

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ANY QUESTIONS?

Resistance to Tanning

Q.—*A man aged 26 is undergoing a course of artificial sunlight. He obstinately refuses to tan and is in consequence perpetually desquamating. He is dark-haired but has a very fair skin. I presume there is a marked lack of pigment which produces this state of affairs. I have had him on iron and the usual prophylactics against peeling, without any improvement. From a psychological point of view I should like him to obtain a good tan. I shall be grateful for any suggestions.*

A.—If the mercury vapour lamp is used a trial might be made of the carbon arc, or of the sun, the rays of which have a deeper penetration into the epidermis. The power of pigmentation if not naturally present cannot be provoked, and fair-skinned people require to be treated by artificial sunlight with caution. Desquamation is the sign of active response of the skin, and tanning the protective result.

Habitual Abortion

Q.—*A woman has had a series of spontaneous abortions and wishes to have a child. How should she be treated?*

A.—The treatment of so-called habitual abortion is largely empirical unless a cause can be found. General systemic disease—particularly nephritis and hypertension—and local pelvic disease—such as retroversion and malformations of the uterus—should be excluded. If no cause is apparent, a recent suggestion has been to have the blood of both husband and wife tested for incompatibility from the point of view of Rh factor. At present this is possible only at a few of the larger laboratories. Syphilis does not cause early abortions, but should be excluded if the abortions have occurred after the twentieth week of pregnancy.

Assuming that such investigations give negative results, then nothing further is necessary until the patient becomes pregnant again. She should be advised to defer pregnancy until six months after the last abortion and to report immediately one menstrual period is missed. No pelvic examination should then be made, but the diagnosis should be established by an Aschheim-Zondek test on the urine. This test may also give some indication of hormone imbalance such as gonadotrophic hormone deficiency. The patient should be instructed to live as quiet a life as possible, avoiding in particular riding in mechanically propelled vehicles, heavy work, and coitus. Various medical forms of treatment have been suggested from time to time, and although definite proof is lacking most clinicians are of the opinion that they have some value. The most commonly employed are progesterone, 2 mg. intramuscularly twice weekly up to the thirty-second week of pregnancy; thyroid, 1 gr. nocte; and vitamin E, 6 mg. once or twice daily until term. These three can be combined with advantage and should be begun as early as possible in pregnancy. In place of progesterone, ethisterone, 5 mg. t.d.s. by mouth, can be given. It has a similar, if less powerful, action on the uterus. Finally, the patient should be assured of an adequate intake of iron, calcium, and vitamins A, B, C, and D. These are conveniently given in the form of a compound tablet.

Antibody in Convalescent Measles Serum

Q.—*Is there any serological method for the estimation of antibody in convalescent measles serum?*

A.—There is none as yet. There is no doubt, of course, that, given a measles antigen, the serological assay of measles serum would be possible. But for a virus antigen to be satisfactory for these serological tests a high concentration of virus is essential. Blood or nasopharyngeal washings from cases of early measles, although virulent, would probably contain insufficient antigen to be of use as an antigen even in a complement-fixation test, which works with a lower "threshold" of antigen than agglutination or precipitation. The recent claim to have cultivated measles virus on the chorio-

allantoic membrane of the developing hen's egg has been confirmed, and this method should make available a suitable measles antigen for serological test.

Drug-resistant Organisms

Q.—*We often read that small doses of the sulphonamides are not only useless but may be harmful in producing a drug-fast strain of organism. Is there any evidence that this belief is a fact? In one of your annotations ("Prophylaxis of Rheumatic Fever," Journal, Dec. 19, 1942, p. 729) one might gather that small doses (1.0 and 1.3 g.) were found helpful over a period of years, and that objectionable results were few. In treating syphilis with N.A.B. some think massive therapy is much more dangerous than the relatively conservative doses extending over months or years. Are the instances comparable?*

A.—Continued exposure to sublethal concentrations of many types of antiseptic substance, ranging from phenol and mercury perchloride even, according to recent evidence, to penicillin, may produce increased resistance to its action. This is due not to a change in the metabolic behaviour of the bacterial cell but to the selective breeding out of those individual cells which possess a greater capacity for resistance. There is both *in vitro* and clinical evidence that this is true of the sulphonamides, and the danger of inadequate dosage is well recognized, particularly in the treatment of pneumonia and gonorrhoea. The treatment of syphilis is not comparable for two main reasons. (1) Although drug-resistant syphilis occurs, there is no proof that a change in the spirochaete due to habituation to arsenical compounds is responsible for it; experimental attempts to produce this change have failed. (2) The extended treatment of syphilis does not consist in giving small doses of the drug three times a day, but in giving large doses at long intervals, following each of which the concentration in the body is high. Such a series of spaced attacks on the micro-organism, each adequate in itself, is quite a different thing from continuous under-dosage.

Vaccine in Pertussis Therapy

Q.—*Is pertussis vaccine of value in the treatment of whooping-cough?*

A.—The consensus in this country is unfavourable to the use of vaccines in the treatment of pertussis. When given in the paroxysmal stage they may even cause an increase in the frequency and severity of the spasms (Begg and Coveney[1]). In America, too, Sauer[2] could find no amelioration of symptoms in either mild or severe cases treated with vaccine. Yet Madsen states that Danish doctors are practically unanimous in claiming that treatment with vaccine will shorten the disease and render it much milder. Some support for this view is given by Thompson,[3] when, following treatment with pertussis "endotoxin," he observed amelioration and shortening of the infection in a group of *early* cases, but no effect among those in whom the disease was well established. His findings were well controlled. Claims have lately been made for the Lederle detoxicated pertussis antigen in the treatment of pertussis, but in a small series of hospital cases Baker[4] failed to confirm any beneficial effects. In summary, it is suggested that vaccine therapy with 0.1 to 0.2 c.cm. doses at 2- or 3-day intervals should not be discouraged in children intimately exposed or in the early catarrhal stage of pertussis.

REFERENCES

1 *Lancet*, 1936, **1**, 82.
2 *J. Amer. med. Ass.*, 1933, **101**, 1449.
3 *Lancet*, 1937, **2**, 733.
4 *British Medical Journal*, 1943, **1**, 562.

Treatment of Gout

Q.—*What is the modern treatment of gout? Has the present-day patient any better prospects from a prognostic point of view than, say, his grandfather had?*

A.—The treatment of this acute condition has not changed, as reliance is still placed on colchicum. This is given in full doses of 15 minims of the tincture combined with 10 to 20 gr. of sodium salicylate and 20 gr. of sodium bicarbonate every 4 hours. This medicine should be kept in the house and given as soon as the joint begins to swell. The prognosis has greatly improved in the last 100 years, as various factors, like lead poisoning and septic foci, which are believed to favour attacks of gout, have been largely eliminated, and the preventive treatment is much improved. Various drugs—cinchophen, aspirin, and calcium aspirin—increase the output of uric acid in the urine. In a severe case 10 gr. of aspirin should be given 3 times a day 3 days each week until the joint has completely recovered. The dose should then be reduced to 2 days each week and later on to 1 a week. This dose may have to be continued indefinitely, or the dose may be reduced to once a month; but the patient should increase the dose as soon as he has any twinge of pain. If aspirin fails to prevent the attacks cinchophen should be used in the same way. It is more apt to cause unpleasant symptoms, like urticaria, nausea, or vomiting, and if these symptoms occur the patient should be told to stop taking it at once as he may develop a hepatitis and jaundice. Physiotherapy may be necessary to enable the joint to recover full movement. Patients should avoid sweetbreads, liver, kidneys, tripe, whitebait, sardines, sprats, and roes of all fishes; and red wines, champagne, and all malt liquors.

The National Bread

Q.—*What is added to wheat flour in the national bread? Is it more nutritious than the pre-war bread? And if calcium is added is this of any nutritive value?*

A.—During the past year several changes have been made in the ingredients of the national loaf. More English wheat is being used than a year ago, and at the present time it comprises 43.6% of the grist. Since Feb. 13 last, barley or a mixture of groats (dehulled oats) and barley has also been included. In May, 1942, calcium carbonate in the form of creta praeparata was added to the flour for the first time, at the rate of 7 oz. per sack of 280 lb., and at the end of April, 1943, approximately 89% of the national flour produced in the United Kingdom was so fortified. Since the middle of March, 1943, the addition of 2 lb. dried skimmed milk per sack has also been general, and over 90% of the flour is now fortified in this way. The chief difference that these additions have made is to the calcium. Pre-war white flour contained 16 mg. per 100 g.; unfortified national flour contained about 21 mg.; and the present flour with its calcium carbonate and skimmed milk contains 93 mg. The amount of calcium being added to the flour is just enough to combine with all the phytic acid in the bread and immobilize it, so that the calcium in the rest of the diet is available for absorption. It is unlikely that much of the calcium added to the bread is absorbed.

The present fortified national loaf is more nutritious than pre-war bread because it contains twice as much of vitamins B_1 and B_2, and a little animal protein from the added skimmed milk. It contains more iron, but it is still an open question whether this is available or not. It seems probable that it is present in the flour as the insoluble ferric phytate and is not absorbed.

"Morton's Metatarsalgia"

Q.—*Physical therapy having failed, will the symptoms of Morton's metatarsalgia continue indefinitely if untreated? Does operation provide a certain cure for this painful complaint?*

A.—Morton's metatarsalgia is not a diagnosis. Nevertheless in the majority of cases the underlying condition is an occupational strain. Physical therapy in all such lesions, though an important aid, is not often the fundamental method of approach. This requires careful search for and alleviation of the stresses to which the limb has been exposed; the removal of aggravating factors such as focal infection and other debilitating conditions; followed by the restoration of muscular control by re-education. The regulation of conditions of work and life, both physical and psychological, and attention to proper footwear, all are of importance. During the early stages of treatment relief to the metatarsal heads should be given by suitable pads applied directly to the feet, or by bars fixed to the soles of the shoes, immediately behind the metatarsal heads. Faradic foot-baths, graduated remedial exercises, etc., will then be more helpful in effecting a cure, which in chronic cases will often be hastened by manipulation under anaesthesia. No other operation should be necessary.

LETTERS, NOTES, ETC.

Sunlight and Desert Sores

Dr. W. J. BURNS SELKIRK (Birmingham) writes: Dr. Henderson (May 29, p. 657) may be interested in an observation by Dr. Eder, California. Children at his sanatorium subject to sunburn effects escaped these if given iron, though they were not anaemic (*Arch. Pediat.*, Dec., 1935, p. 833, quoted by *Med. Pr.*, Feb. 26, 1936).

A Spanish–English Medical Dictionary

Dr. M. G. MCELLIGOTT (Heathwood, Bushey Heath, Herts) writes to say that he has compiled a Spanish–English Medical Dictionary, which is now almost complete and of which the dedication has been accepted by an eminent Spanish surgeon. This work should fill a distinct need at the present time, but it awaits a publisher. Dr. McElligott would welcome any hints from Spanish-speaking readers which might make the dictionary more useful.

Welfare of Laboratory Animals

The Universities Federation for Animal Welfare (U.F.A.W.) is collecting information on: (1) anaesthesia of rats, rabbits, guinea-pigs, etc.; (2) methods of killing laboratory animals; and (3) living conditions, housing, diet, etc., of such animals. Views and suggestions should be sent to the Federation at its temporary address, 284, Regent's Park Road, N.3. A small panel of experienced persons will advise on the collected material. It is hoped that this pooling of the experience of those engaged in experiments on animals will enable the maximum of consideration to be given to the welfare of laboratory animals.

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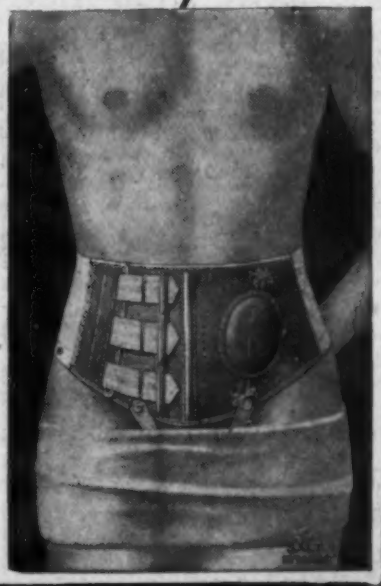

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